

<120> RECOMBINANT VACCINE AGAINST BOTULINUM NEUROTOXIN

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<130> A33626-A 067252.0107
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<140> 09/611,419

<141> 2000-07-06

<150> PCT/US00/12890

<151> 2000-05-12

<150> 60/133,865

<151> 1999-05-12

<150> 60/133,866

<151> 1999-05-12

<150> 60/133,867

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<151> 1999-05-12

<150> 60/133,869

<151> 1999-05-12

<150> 60/146,192

<151> 1999-07-29

<160> 42

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 1332

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic construct based on BoNTA Hc

<221> CDS

<222> (13)...(1326)

<400> 1

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Met Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Asn

1 5 10

atc atc aat acc tcc atc ctg aac ctg cgc tac gaa tcc aat cac ctg

Ile	Ile 15	Asn	Thr	Ser	Ile	Leu 20	Asn	Leu	Arg	Tyr	Glu 25	Ser	Asn	His	Leu		
	_	_		_		gct Ala									_	147	
					_	aag Lys		_		_	_			_	-	195	
				_	_	atc Ile	_	_		_		_				243	
						acc Thr										291	
						aac Asn 100										339	
						aaa Lys										387	
						cag Gln										435	
						atc Ile										483	
						cgt Arg										531	
ggc Gly	cgt Arg 175	ctg Leu	atc Ile	gac Asp	cag Gln	aaa Lys 180	ccg Pro	atc Ile	tcc Ser	aat Asn	ctg Leu 185	ggt Gly	aac Asn	atc Ile	cac His	579	
gct Ala 190	tct Ser	aat Asn	aac Asn	atc Ile	atg Met 195	ttc Phe	aaa Lys	ctg Leu	gac Asp	ggt Gly 200	tgt Cys	cgt Arg	gac Asp	act Thr	cac His 205	627	
cgc Arg	tac Tyr	atc Ile	tgg Trp	atc Ile 210	aaa Lys	tac Tyr	ttc Phe	aat Asn	ctg Leu 215	ttc Phe	gac Asp	aaa Lys	gaa Glu	ctg Leu 220	aac Asn	675	
gaa Glu	aaa Lys	gaa Glu	atc Ile 225	aaa Lys	gac Asp	ctg Leu	tac Tyr	gac Asp 230	aac Asn	cag Gln	tcc Ser	aat Asn	tct Ser 235	ggt Gly	atc Ile	723	
						gac Asp										771	

					gat Asp					-	-	_			_	819
					atg Met 275											867
					ctg Leu											915
					gcg Ala											963
					atc Ile											1011
ctg Leu	gct Ala 335	acc Thr	aat Asn	gct Ala	tct Ser	cag Gln 340	gct Ala	ggt Gly	gta Val	gaa Glu	aag Lys 345	atc Ile	ttg Leu	tct Ser	gct Ala	1059
					gtt Val 355											1107
					ggt Gly											1155
					gat Asp											1203
					gtt Val											1251
cgt Arg	tcc Ser 415	tct Ser	cgc Arg	act Thr	ctg Leu	ggt Gly 420	tgc Cys	tct Ser	tgg Trp	gag Glu	ttc Phe 425	atc Ile	ccg Pro	gtt Val	gat Asp	1299
					cgt Arg 435				gaat	tc						1332

<210> 2

<211> 437

<212> PRT

<213> Artificial Sequence

<220>

<400> 2 Met Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Asn Ile Ile Asn Thr Ser Ile Leu Asn Leu Arg Tyr Glu Ser Asn His Leu Ile Asp Leu 25 Ser Arg Tyr Ala Ser Lys Ile Asn Ile Gly Ser Lys Val Asn Phe Asp 40 Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu Ser Ser Lys 60 Ile Glu Val Ile Leu Lys Asn Ala Ile Val Tyr Asn Ser Met Tyr Glu Asn Phe Ser Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr Phe Asn Ser 90 Ile Ser Leu Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Glu Asn Asn 105 Ser Gly Trp Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile Trp Thr Leu 120 Gln Asp Thr Gln Glu Ile Lys Gln Arg Val Val Phe Lys Tyr Ser Gln 135 140 Met Ile Asn Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe Val Thr Ile 150 155 Thr Asn Asn Arg Leu Asn Asn Ser Lys Ile Tyr Ile Asn Gly Arg Leu 165 170 Ile Asp Gln Lys Pro Ile Ser Asn Leu Gly Asn Ile His Ala Ser Asn 185 Asn Ile Met Phe Lys Leu Asp Gly Cys Arg Asp Thr His Arg Tyr Ile 200 Trp Ile Lys Tyr Phe Asn Leu Phe Asp Lys Glu Leu Asn Glu Lys Glu 215 220 Ile Lys Asp Leu Tyr Asp Asn Gln Ser Asn Ser Gly Ile Leu Lys Asp 230 235 Phe Trp Gly Asp Tyr Leu Gln Tyr Asp Lys Pro Tyr Tyr Met Leu Asn 245 250 Leu Tyr Asp Pro Asn Lys Tyr Val Asp Val Asn Asn Val Gly Ile Arg 260 265 Gly Tyr Met Tyr Leu Lys Gly Pro Arg Gly Ser Val Met Thr Thr Asn 280 Ile Tyr Leu Asn Ser Ser Leu Tyr Arg Gly Thr Lys Phe Ile Ile Lys 295 300 Lys Tyr Ala Ser Gly Asn Lys Asp Asn Ile Val Arg Asn Asn Asp Arg 310 315 Val Tyr Ile Asn Val Val Lys Asn Lys Glu Tyr Arg Leu Ala Thr 325 330 Asn Ala Ser Gln Ala Gly Val Glu Lys Ile Leu Ser Ala Leu Glu Ile 345 Pro Asp Val Gly Asn Leu Ser Gln Val Val Val Met Lys Ser Lys Asn 360 Asp Gln Gly Ile Thr Asn Lys Cys Lys Met Asn Leu Gln Asp Asn Asn 375 Gly Asn Asp Ile Gly Phe Ile Gly Phe His Gln Phe Asn Asn Ile Ala 390 Lys Leu Val Ala Ser Asn Trp Tyr Asn Arg Gln Ile Glu Arg Ser Ser 410 Arg Thr Leu Gly Cys Ser Trp Glu Phe Ile Pro Val Asp Asp Gly Trp



420 425 430

Gly Glu Arg Pro Leu 435

<210> 3

<211> 1323

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic construct based on BoNTA Hc

<221> CDS

<222> (13) ... (1314)

<400> 3

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1 5 10

acc tcc atc ctg aac ctg cgc tac gaa tcc aat cac ctg atc gac ctg 99
Thr Ser Ile Leu Asn Leu Arg Tyr Glu Ser Asn His Leu Ile Asp Leu
15 20 25

tct cgc tac gct tcc aaa atc aac atc ggt tct aaa gtt aac ttc gat 14'
Ser Arg Tyr Ala Ser Lys Ile Asn Ile Gly Ser Lys Val Asn Phe Asp
30 35 40 45

ccg atc gac aag aat cag atc cag ctg ttc aat ctg gaa tct tcc aaa 195
Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu Ser Ser Lys

atc gaa gtt atc ctg aag aat gct atc gta tac aac tct atg tac gaa 243
Ile Glu Val Ile Leu Lys Asn Ala Ile Val Tyr Asn Ser Met Tyr Glu
65 70 75

aac ttc tcc acc tcc ttc tgg atc cgt atc ccg aaa tac ttc aac tcc 291
Asn Phe Ser Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr Phe Asn Ser

atc tct ctg aac aat gaa tac acc atc atc aac tgc atg gaa aac aat 339
Ile Ser Leu Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Glu Asn Asn
95 100 105

tct ggt tgg aaa gta tct ctg aac tac ggt gaa atc atc tgg act ctg 387 Ser Gly Trp Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile Trp Thr Leu 110 115 120 125

cag gac act cag gaa atc aaa cag cgt gtt gta ttc aaa tac tct cag 435 Gln Asp Thr Gln Glu Ile Lys Gln Arg Val Val Phe Lys Tyr Ser Gln 130 135 140

atg atc aac atc tct gac tac atc aat cgc tgg atc ttc gtt acc atc 483
Met Ile Asn Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe Val Thr Ile
145
150
155



		aac Asn															531
		gac Asp 175															579
		atc Ile															627
		atc Ile															675
		aaa Lys															723
		tgg Trp															771
Ğ		tac Tyr 255															819
)		tac Tyr															867
		tac Tyr															915
	aaa Lys	tac Tyr	gcg Ala	tct Ser 305	ggt Gly	aac Asn	aag Lys	gac Asp	aat Asn 310	atc Ile	gtt Val	cgc Arg	aac Asn	aat Asn 315	gat Asp	cgt Arg	963
		tac Tyr															1011
		gct Ala 335															1059
	ccg Pro 350	gac Asp	gtt Val	ggt Gly	aat Asn	ctg Leu 355	tct Ser	cag Gln	gta Val	gtt Val	gta Val 360	atg Met	aaa Lys	tcc Ser	aag Lys	aac Asn 365	1107
		cag Gln															1155
	ggt	aac	gat	atc	ggt	ttc	atc	ggt	ttc	cac	cag	ttc	aac	aat	atc	gct	1203

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Gly Asn Asp Ile Gly Phe Ile Gly Phe His Gln Phe Asn Asn Ile Ala
aaa ctg gtt gct tcc aac tgg tac aat cgt cag atc gaa cgt tcc tct
                                                                    1251
Lys Leu Val Ala Ser Asn Trp Tyr Asn Arg Gln Ile Glu Arg Ser Ser
        400
cgc act ctg ggt tgc tct tgg gag ttc atc ccg gtt gat gac ggt tgg
                                                                    1299
Arg Thr Leu Gly Cys Ser Trp Glu Phe Ile Pro Val Asp Asp Gly Trp
                        420
ggt gaa cgt ccg ctg taagaattc
                                                                    1323
Gly Glu Arg Pro Leu
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<210> 4
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<212> PRT
<213> Artificial Sequence
<223> Encoded polypeptide of a synthetic construct based
      on BoNTA Hc
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Leu Asn Leu Arg Tyr Glu Ser Asn His Leu Ile Asp Leu Ser Arg Tyr
Ala Ser Lys Ile Asn Ile Gly Ser Lys Val Asn Phe Asp Pro Ile Asp
                            40
Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu Ser Ser Lys Ile Glu Val
                        55
Ile Leu Lys Asn Ala Ile Val Tyr Asn Ser Met Tyr Glu Asn Phe Ser
                    70
                                         75
Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr Phe Asn Ser Ile Ser Leu
                85
                                     90
Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Glu Asn Asn Ser Gly Trp
                                105
Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile Trp Thr Leu Gln Asp Thr
                            120
                                                 125
Gln Glu Ile Lys Gln Arg Val Val Phe Lys Tyr Ser Gln Met Ile Asn
                        135
                                             140
Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe Val Thr Ile Thr Asn Asn
                    150
                                        155
Arg Leu Asn Asn Ser Lys Ile Tyr Ile Asn Gly Arg Leu Ile Asp Gln
                165
                                     170
Lys Pro Ile Ser Asn Leu Gly Asn Ile His Ala Ser Asn Asn Ile Met
            180
                                185
Phe Lys Leu Asp Gly Cys Arg Asp Thr His Arg Tyr Ile Trp Ile Lys
                            200
Tyr Phe Asn Leu Phe Asp Lys Glu Leu Asn Glu Lys Glu Ile Lys Asp
                        215
Leu Tyr Asp Asn Gln Ser Asn Ser Gly Ile Leu Lys Asp Phe Trp Gly
Asp Tyr Leu Gln Tyr Asp Lys Pro Tyr Tyr Met Leu Asn Leu Tyr Asp
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245
                                     250
                                                         255
Pro Asn Lys Tyr Val Asp Val Asn Asn Val Gly Ile Arg Gly Tyr Met
                                 265
Tyr Leu Lys Gly Pro Arg Gly Ser Val Met Thr Thr Asn Ile Tyr Leu
                             280
                                                 285
Asn Ser Ser Leu Tyr Arg Gly Thr Lys Phe Ile Ile Lys Lys Tyr Ala
                        295
                                             300
Ser Gly Asn Lys Asp Asn Ile Val Arg Asn Asn Asp Arg Val Tyr Ile
                    310
                                         315
Asn Val Val Lys Asn Lys Glu Tyr Arg Leu Ala Thr Asn Ala Ser
                325
                                     330
Gln Ala Gly Val Glu Lys Ile Leu Ser Ala Leu Glu Ile Pro Asp Val
                                 345
Gly Asn Leu Ser Gln Val Val Wet Lys Ser Lys Asn Asp Gln Gly
                            360
Ile Thr Asn Lys Cys Lys Met Asn Leu Gln Asp Asn Asn Gly Asn Asp
                                             380
Ile Gly Phe Ile Gly Phe His Gln Phe Asn Asn Ile Ala Lys Leu Val
                    390
                                        395
Ala Ser Asn Trp Tyr Asn Arg Gln Ile Glu Arg Ser Ser Arg Thr Leu
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                                    410
Gly Cys Ser Trp Glu Phe Ile Pro Val Asp Asp Gly Trp Gly Glu Arg
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Pro Leu
<210> 5
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<212> DNA
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<400> 5

<220>
<223> Synthetic construct based on BoNTA Hc
<221> CDS
<222> (13)...(1317)

<213> Artificial Sequence

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aat acc tcc atc ctg aac ctg cgc tac gaa tcc aat cac ctg atc gac 99
Asn Thr Ser Ile Leu Asn Leu Arg Tyr Glu Ser Asn His Leu Ile Asp
15 20 25

ctg tct cgc tac gct tcc aaa atc aac atc ggt tct aaa gtt aac ttc 147 Leu Ser Arg Tyr Ala Ser Lys Ile Asn Ile Gly Ser Lys Val Asn Phe 30 45

gat ccg atc gac aag aat cag atc cag ctg ttc aat ctg gaa tct tcc 195
Asp Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu Ser Ser
50 55 60

aaa atc gaa gtt atc ctg aag aat gct atc gta tac aac tct atg tac 243 Lys Ile Glu Val Ile Leu Lys Asn Ala Ile Val Tyr Asn Ser Met Tyr

-									_		_			ttc Phe		291
														gaa Glu		339
					-		_				_			tgg Trp		387
														tac Tyr 140		435
														gtt Val		483
														ggc Gly		531
														gct Ala		579
Asn 190	Asn	Ile	Met	Phe	Lys 195	Leu	Asp	Gly	Cys	Arg 200	Asp	Thr	His	cgc Arg	Tyr 205	627
Ile	Trp	Ile	Lys	Tyr 210	Phe	Asn	Leu	Phe	Asp 215	Lys	Glu	Leu	Asn	gaa Glu 220	Lys	675
Glu	Ile	Lys	Asp 225	Leu	Tyr	Asp	Asn	Gln 230	Ser	Asn	Ser	Gly	Ile 235	ctg Leu	Lys	723
Asp	Phe	Trp 240	Gly	Asp	Tyr	Leu	Gln 245	Tyr	Asp	Lys	Pro	Tyr 250	Tyr	atg Met	Leu	771
aat Asn	ctg Leu 255	tac Tyr	gat Asp	ccg Pro	aac Asn	aaa Lys 260	tac Tyr	gtt Val	gac Asp	gtc Val	aac Asn 265	aat Asn	gta Val	ggt Gly	atc Ile	819
Arg 270	Gly	Tyr	Met	Tyr	Leu 275	Lys	Gly	Pro	Arg	Gly 280	Ser	Val	Met	act Thr	Thr 285	867
aac Asn	atc Ile	tac Tyr	ctg Leu	aac Asn 290	tct Ser	tcc Ser	ctg Leu	tac Tyr	cgt Arg 295	ggt Gly	acc Thr	aaa Lys	ttc Phe	atc Ile 300	atc Ile	915

					ggt Gly											963
					gtt Val	_	-	_			_		_	_	_	1011
					gct Ala											1059
					aat Asn 355											1107
					act Thr											1155
					ggt Gly											1203
					tcc Ser											1251
					tgc Cys											1299
		gaa Glu	_	_	ctg Leu 435	taag	gaatt	c			٠					1326
<212	L> 43 2> PF	TΣ	cial	. Sec	quenc	:e										
<220 <223	3 > Er	icode			eptid	le of	as	yntl	netio	c con	ıstru	ıct b	ased	l		
<400)> 6															
		Ser	Thr	Phe 5	Thr	Glu	Tyr	Ile	Lys 10	Asn	Ile	Ile	Asn	Thr 15	Ser	
	Leu	Asn		-	Tyr	Glu	Ser			Leu	Ile	Asp			Arg	
Tyr	Ala		20 Lys	Ile	Asn	Ile		25 Ser	Lys	Val	Asn		30 Asp	Pro	Ile	
Asp		35 Asn	Gln	Ile	Gln		40 Phe	Asn	Leu	Glu		45 Ser	Lys	Ile	Glu	
Val	50 Ile	Leu	Lys	Asn	Ala	55 Ile	Val	Tyr	Asn	Ser	60 Met	Tyr	Glu	Asn	Phe	

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70
Ser Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr Phe Asn Ser Ile Ser
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Leu Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Glu Asn Asn Ser Gly
                                105
Trp Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile Trp Thr Leu Gln Asp
                            120
Thr Gln Glu Ile Lys Gln Arg Val Val Phe Lys Tyr Ser Gln Met Ile
                        135
                                            140
Asn Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe Val Thr Ile Thr Asn
                   150
Asn Arg Leu Asn Asn Ser Lys Ile Tyr Ile Asn Gly Arg Leu Ile Asp
                                    170
Gln Lys Pro Ile Ser Asn Leu Gly Asn Ile His Ala Ser Asn Asn Ile
                                185
Met Phe Lys Leu Asp Gly Cys Arg Asp Thr His Arg Tyr Ile Trp Ile
                            200
Lys Tyr Phe Asn Leu Phe Asp Lys Glu Leu Asn Glu Lys Glu Ile Lys
                        215
                                            220
Asp Leu Tyr Asp Asn Gln Ser Asn Ser Gly Ile Leu Lys Asp Phe Trp
                    230
                                        235
Gly Asp Tyr Leu Gln Tyr Asp Lys Pro Tyr Tyr Met Leu Asn Leu Tyr
                245
                                    250
Asp Pro Asn Lys Tyr Val Asp Val Asn Asn Val Gly Ile Arg Gly Tyr
                                265
Met Tyr Leu Lys Gly Pro Arg Gly Ser Val Met Thr Thr Asn Ile Tyr
                            280
Leu Asn Ser Ser Leu Tyr Arg Gly Thr Lys Phe Ile Ile Lys Lys Tyr
                        295
                                            300
Ala Ser Gly Asn Lys Asp Asn Ile Val Arg Asn Asn Asp Arg Val Tyr
                    310
                                        315
Ile Asn Val Val Lys Asn Lys Glu Tyr Arg Leu Ala Thr Asn Ala
                325
                                    330
Ser Gln Ala Gly Val Glu Lys Ile Leu Ser Ala Leu Glu Ile Pro Asp
                                345
Val Gly Asn Leu Ser Gln Val Val Val Met Lys Ser Lys Asn Asp Gln
       355
                           360
                                             365
Gly Ile Thr Asn Lys Cys Lys Met Asn Leu Gln Asp Asn Asn Gly Asn
                        375
Asp Ile Gly Phe Ile Gly Phe His Gln Phe Asn Asn Ile Ala Lys Leu
                    390
Val Ala Ser Asn Trp Tyr Asn Arg Gln Ile Glu Arg Ser Ser Arg Thr
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Leu Gly Cys Ser Trp Glu Phe Ile Pro Val Asp Asp Gly Trp Gly Glu
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Arg Pro Leu
        435
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<210> 7

<211> 1341

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic construct based on BoNTA Hc

<221> CDS <222> (10)...(1329)

<400> 7

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ctg aac ctg cgt tac aaa gac aac aat ctg atc gat ctg tct ggt tac 99
Leu Asn Leu Arg Tyr Lys Asp Asn Asn Leu Ile Asp Leu Ser Gly Tyr
15 20 25 30

ggt gct aaa gtt gaa gta tac gac ggt gtt gaa ctg aat gac aag aac 147 Gly Ala Lys Val Glu Val Tyr Asp Gly Val Glu Leu Asn Asp Lys Asn 35 40 45

cag ttc aaa ctg acc tct tcc gct aac tct aag atc cgt gtt act cag $\,$ 195 Gln Phe Lys Leu Thr Ser Ser Ala Asn Ser Lys Ile Arg Val Thr Gln $\,$ 50 $\,$ 55 $\,$ 60

aat cag aac atc atc ttc aac tcc gta ttc ctg gac ttc tct gtt tcc 243
Asn Gln Asn Ile Ile Phe Asn Ser Val Phe Leu Asp Phe Ser Val Ser
65 70 75

ttc tgg atc cgt atc ccg aaa tac aag aac gac ggt atc cag aat tac 291
Phe Trp Ile Arg Ile Pro Lys Tyr Lys Asn Asp Gly Ile Gln Asn Tyr
80 85 90

atc cac aat gaa tac acc atc atc aac tgc atg aag aat aac tct ggt

Ile His Asn Glu Tyr Thr Ile Ile Asn Cys Met Lys Asn Asn Ser Gly

95

100

105

tgg aag atc tcc atc cgc ggt aac cgt atc atc tgg act ctg atc gat 387
Trp Lys Ile Ser Ile Arg Gly Asn Arg Ile Ile Trp Thr Leu Ile Asp
115 120 125

atc aac ggt aag acc aaa tct gta ttc ttc gaa tac aac atc cgt gaa 435
Ile Asn Gly Lys Thr Lys Ser Val Phe Phe Glu Tyr Asn Ile Arg Glu
130 135 140

gac atc tct gaa tac atc aat cgc tgg ttc ttc gtt acc atc acc aat 483 Asp Ile Ser Glu Tyr Ile Asn Arg Trp Phe Phe Val Thr Ile Thr Asn 145 150 155

aac ctg aac aat gct aaa atc tac atc aac ggt aaa ctg gaa tct aat 531 Asn Leu Asn Asn Ala Lys Ile Tyr Ile Asn Gly Lys Leu Glu Ser Asn 160 165 170

acc gac atc aaa gac atc cgt gaa gtt atc gct aac ggt gaa atc atc
Thr Asp Ile Lys Asp Ile Arg Glu Val Ile Ala Asn Gly Glu Ile Ile

ttc aaa ctg gac ggt gac atc gat cgt acc cag ttc atc tgg atg aaa 627
Phe Lys Leu Asp Gly Asp Ile Asp Arg Thr Gln Phe Ile Trp Met Lys
195 200 205

tac ttc tcc atc ttc aac acc gaa ctg tct cag tcc aat atc gaa gaa 679



	Tyr	Phe	Ser	Ile 210	Phe	Asn	Thr	Glu	Leu 215	Ser	Gln	Ser	Asn	Ile 220	Glu	Glu	
													gac Asp 235				723
													aat Asn				771
													gtt Val				819
													atc Ile				867
													aaa Lys				915
	cag Gln	tcc Ser	atc Ile 305	aat Asn	gat Asp	gac Asp	atc Ile	gta Val 310	cgt Arg	aaa Lys	gaa Glu	gac Asp	tac Tyr 315	atc Ile	tac Tyr	ctg Leu	963
	gac Asp	ttc Phe 320	ttc Phe	aac Asn	ctg Leu	aat Asn	cag Gln 325	gaa Glu	tgg Trp	cgt Arg	gta Val	tac Tyr 330	acc Thr	tac Tyr	aag Lys	tac Tyr	1011
	ttc Phe 335	aag Lys	aaa Lys	gaa Glu	gaa Glu	gaa Glu 340	aag Lys	ctt Leu	ttc Phe	ctg Leu	gct Ala 345	ccg Pro	atc Ile	tct Ser	gat Asp	tcc Ser 350	1059
\bigcirc	gac Asp	gaa Glu	ctc Leu	tac Tyr	aac Asn 355	acc Thr	atc Ile	cag Gln	atc Ile	aaa Lys 360	gaa Glu	tac Tyr	gac Asp	gaa Glu	cag Gln 365	ccg Pro	1107
	acc Thr	tac Tyr	tct Ser	tgc Cys 370	cag Gln	ctg Leu	ctg Leu	ttc Phe	aag Lys 375	aaa Lys	gat Asp	gaa Glu	gaa Glu	tct Ser 380	act Thr	gac Asp	1155
	gaa Glu	atc Ile	ggt Gly 385	ctg Leu	atc Ile	ggt Gly	atc Ile	cac His 390	cgt Arg	ttc Phe	tac Tyr	gaa Glu	tct Ser 395	ggt Gly	atc Ile	gta Val	1203
	Phe	gaa Glu 400	gaa Glu	tac Tyr	aaa Lys	gac Asp	tac Tyr 405	ttc Phe	tgc Cys	atc Ile	tcc Ser	aaa Lys 410	tgg Trp	tac Tyr	ctg Leu	aag Lys	1251
	gaa Glu 415	gtt Val	aaa Lys	cgc Arg	aaa Lys	ccg Pro 420	tac Tyr	aac Asn	ctg Leu	Lys	ctg Leu 425	ggt Gly	tgc Cys	aat Asn	Trp	cag Gln 430	1299
	ttc Phe	atc Ile	ccg Pro	aaa Lys	gac Asp	gaa Glu	ggt Gly	tgg Trp	acc Thr	gaa Glu	tagt	aaga	at t	С			1341

435 440

<210> 8 <211> 440

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<212> PRT
<213> Artificial Sequence
<220>
<223> Encoded polypeptide of a synthetic construct based
      on BoNTB Hc
<400> 8
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Leu Arg Tyr Lys Asp Asn Asn Leu Ile Asp Leu Ser Gly Tyr Gly Ala
Lys Val Glu Val Tyr Asp Gly Val Glu Leu Asn Asp Lys Asn Gln Phe
                            40
Lys Leu Thr Ser Ser Ala Asn Ser Lys Ile Arg Val Thr Gln Asn Gln
                                            60
Asn Ile Ile Phe Asn Ser Val Phe Leu Asp Phe Ser Val Ser Phe Trp
                    70
                                        75
Ile Arg Ile Pro Lys Tyr Lys Asn Asp Gly Ile Gln Asn Tyr Ile His
                                    90
Asn Glu Tyr Thr Ile Ile Asn Cys Met Lys Asn Asn Ser Gly Trp Lys
                                105
Ile Ser Ile Arg Gly Asn Arg Ile Ile Trp Thr Leu Ile Asp Ile Asn
                            120
Gly Lys Thr Lys Ser Val Phe Phe Glu Tyr Asn Ile Arg Glu Asp Ile
                        135
                                            140
Ser Glu Tyr Ile Asn Arg Trp Phe Phe Val Thr Ile Thr Asn Asn Leu
                    150
                                        155
Asn Asn Ala Lys Ile Tyr Ile Asn Gly Lys Leu Glu Ser Asn Thr Asp
                165 .
                                    170
Ile Lys Asp Ile Arg Glu Val Ile Ala Asn Gly Glu Ile Ile Phe Lys
            180
                               185
Leu Asp Gly Asp Ile Asp Arg Thr Gln Phe Ile Trp Met Lys Tyr Phe
                            200
Ser Ile Phe Asn Thr Glu Leu Ser Gln Ser Asn Ile Glu Glu Arg Tyr
                        215
                                            220
Lys Ile Gln Ser Tyr Ser Glu Tyr Leu Lys Asp Phe Trp Gly Asn Pro
                    230
                                        235
Leu Met Tyr Asn Lys Glu Tyr Tyr Met Phe Asn Ala Gly Asn Lys Asn
                                    250
Ser Tyr Ile Lys Leu Lys Lys Asp Ser Pro Val Gly Glu Ile Leu Thr
                                265
Arg Ser Lys Tyr Asn Gln Asn Ser Lys Tyr Ile Asn Tyr Arg Asp Leu
                            280
                                                285
Tyr Ile Gly Glu Lys Phe Ile Ile Arg Arg Lys Ser Asn Ser Gln Ser
                        295
Ile Asn Asp Asp Ile Val Arg Lys Glu Asp Tyr Ile Tyr Leu Asp Phe
                    310
                                        315
Phe Asn Leu Asn Gln Glu Trp Arg Val Tyr Thr Tyr Lys Tyr Phe Lys
                                    330
Lys Glu Glu Lys Leu Phe Leu Ala Pro Ile Ser Asp Ser Asp Glu
            340
                                345
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Leu Tyr Asn Thr Ile Gln Ile Lys Glu Tyr Asp Glu Gln Pro Thr Tyr
                            360
Ser Cys Gln Leu Leu Phe Lys Lys Asp Glu Glu Ser Thr Asp Glu Ile
                        375
Gly Leu Ile Gly Ile His Arg Phe Tyr Glu Ser Gly Ile Val Phe Glu
                    390
                                       395
Glu Tyr Lys Asp Tyr Phe Cys Ile Ser Lys Trp Tyr Leu Lys Glu Val
                405
                                   410
Lys Arg Lys Pro Tyr Asn Leu Lys Leu Gly Cys Asn Trp Gln Phe Ile
                               425
Pro Lys Asp Glu Gly Trp Thr Glu
        435
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<211> 1371
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<221> CDS
<222> (10)...(1359)
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Met Thr Ile Pro Phe Asn Ile Phe Ser Tyr Thr Asn Asn Ser
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ctg. ttg.aag. gac.atc.aac gag tac ttc.aac aac atc aac gac tcc
                                                                 99
Leu Leu Lys Asp Ile Ile Asn Glu Tyr Phe Asn Asn Ile Asn Asp Ser
 15
                    20
aag atc ctg tcc ctg cag aac cgt aag aac acc ttg gtc gac acc tcc
                                                                 147
Lys Ile Leu Ser Leu Gln Asn Arg Lys Asn Thr Leu Val Asp Thr Ser
                35
ggt tac aac gcc gag gtc tcc gag gag ggt gac gtc cag ctg aac cca
                                                                 195
Gly Tyr Asn Ala Glu Val Ser Glu Glu Gly Asp Val Gln Leu Asn Pro
            50
ate tte eea tte gae tte aag etg ggt tee tee ggt gag gae aga ggt
                                                                243
Ile Phe Pro Phe Asp Phe Lys Leu Gly Ser Ser Gly Glu Asp Arg Gly
        65
aag gtc atc gtc acc cag aac gag aac atc gtc tac aac tcc atg tac
                                                                 291
Lys Val Ile Val Thr Gln Asn Glu Asn Ile Val Tyr Asn Ser Met Tyr
gag tee the tee ate tee the tag ate aga ate aae aag tag ate tee
                                                                 339
Glu Ser Phe Ser Ile Ser Phe Trp Ile Arg Ile Asn Lys Trp Val Ser
                   100
                                       105
aac ttg cca ggt tac acc atc atc gac tcc gtc aag aac aac tcc ggt
                                                                387
Asn Leu Pro Gly Tyr Thr Ile Ile Asp Ser Val Lys Asn Asn Ser Gly
               115
                                   120
                                                       125
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			atc Ile								435
	 _	_	cag Gln					_			483
Asn			aac Asn								531
			aag Lys 180				-	_		_	579
			ttg Leu								627
			atc Ile								675
			tgg Trp								723
			atc Ile		_			_	_		771
			tac Tyr 260								819
			atc Ile								867
			ttc Phe								915
			atc Ile								963
			ggt Gly								1011
			ctg Leu 340								1059

				_	atc Ile		_		 _	_		_		1107
_	_		_		atc Ile			_	_		_			1155
			_		cag Gln			_						1203
				_	tcc Ser 405				_		_	_		1251
					aac Asn									1299
		_	_	_	gag Glu								_	1347
	gtc Val		 taat	agga	at t	:c				-				1371

<210> 10 <211> 450 <212> PRT <213> Artificial Sequence

<220>

<400> 10

<223> Encoded polypeptide of a synthetic construct based on BoNTC Hc

Met Thr Ile Pro Phe Asn Ile Phe Ser Tyr Thr Asn Asn Ser Leu Leu 10 Lys Asp Ile Ile Asn Glu Tyr Phe Asn Asn Ile Asn Asp Ser Lys Ile 25 Leu Ser Leu Gln Asn Arg Lys Asn Thr Leu Val Asp Thr Ser Gly Tyr Asn Ala Glu Val Ser Glu Glu Gly Asp Val Gln Leu Asn Pro Ile Phe 55 Pro Phe Asp Phe Lys Leu Gly Ser Ser Gly Glu Asp Arg Gly Lys Val 70 75 Ile Val Thr Gln Asn Glu Asn Ile Val Tyr Asn Ser Met Tyr Glu Ser 85 90 Phe Ser Ile Ser Phe Trp Ile Arg Ile Asn Lys Trp Val Ser Asn Leu 105 Pro Gly Tyr Thr Ile Ile Asp Ser Val Lys Asn Asn Ser Gly Trp Ser 120 125 Ile Gly Ile Ile Ser Asn Phe Leu Val Phe Thr Leu Lys Gln Asn Glu 130 135 140

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Asp Ser Glu Gln Ser Ile Asn Phe Ser Tyr Asp Ile Ser Asn Asn Ala
145
                    150
                                         155
Pro Gly Tyr Asn Lys Trp Phe Phe Val Thr Val Thr Asn Asn Met Met
                                    170
Gly Asn Met Lys Ile Tyr Ile Asn Gly Lys Leu Ile Asp Thr Ile Lys
                                185
Val Lys Glu Leu Thr Gly Ile Asn Phe Ser Lys Thr Ile Thr Phe Glu
                            200
                                                 205
Ile Asn Lys Ile Pro Asp Thr Gly Leu Ile Thr Ser Asp Ser Asp Asn
                        215
Ile Asn Met Trp Ile Arg Asp Phe Tyr Ile Phe Ala Lys Glu Leu Asp
                    230
                                         235
Gly Lys Asp Ile Asn Ile Leu Phe Asn Ser Leu Gln Tyr Thr Asn Val
                                     250
Val Lys Asp Tyr Trp Gly Asn Asp Leu Arg Tyr Asn Lys Glu Tyr Tyr
            260
                                265
Met Val Asn Ile Asp Tyr Leu Asn Arg Tyr Met Tyr Ala Asn Ser Arg
                            280
                                                 285
Gln Ile Val Phe Asn Thr Arg Arg Asn Asn Asp Phe Asn Glu Gly
                        295
                                            300
Tyr Lys Ile Ile Ile Lys Arg Ile Arg Gly Asn Thr Asn Asp Thr Arg
                    310
                                        315
Val Arg Gly Gly Asp Ile Leu Tyr Phe Asp Met Thr Ile Asn Asn Lys
                                    330
Ala Tyr Asn Leu Phe Met Lys Asn Glu Thr Met Tyr Ala Asp Asn His
            340
                                345
Ser Thr Glu Asp Ile Tyr Ala Ile Gly Leu Arg Glu Gln Thr Lys Asp
                            360
Ile Asn Asp Asn Ile Ile Phe Gln Ile Gln Pro Met Asn Asn Thr Tyr
                        375
Tyr Tyr Ala Ser Gln Ile Phe Lys Ser Asn Phe Asn Gly Glu Asn Ile
                    390
                                        395
Ser Gly Ile Cys Ser Ile Gly Thr Tyr Arg Phe Arg Leu Gly Gly Asp
                405
                                    410
Trp Tyr Arg His Asn Tyr Leu Val Pro Thr Val Lys Gln Gly Asn Tyr
            420
                                425
Ala Ser Leu Leu Glu Ser Thr Ser Thr His Trp Gly Phe Val Pro Val
                            440
Ser Glu
    450
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<211> 1374
<212> DNA
<213> Artificial Sequence
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<221> CDS
<222> (10)...(1362)
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          Met Arg Leu Lys Ala Lys Val Asn Glu Ser Phe Glu Asn Thr
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_						tcc Ser						_	_	_	_	99
						aac Asn				_		_		_		147
			_	_		gcc Ala	_	_	_						_	195
		_	_		_	aac Asn	_	_	_							243
						tcc Ser 85										291
Asn 95	Asn	Ile	Leu	Tyr	Ser 100	gcc Ala	Ile	Tyr	Glu	Asn 105	Ser	Ser	Val	Ser	Phe 110	339
Trp	Ile	Lys	Ile	Ser 115	Lys	gac Asp	Leu	Thr	Asn 120	Ser	His	Asn	Glu	Tyr 125	Thr	387
Ile	Ile	Asn	Ser 130	Ile	Glu	cag Gln	Asn	Ser 135	Gly	Trp	Lys	Leu	Cys 140	Ile	Arg	435
Asn	Gly	Asn 145	Ile	Glu	Trp	atc Ile	Leu 150	Gln	Asp	Val	Asn	Arg 155	Lys	Tyr	Lys	483
Ser	Leu 160	Ile	Phe	Asp	Tyr	tcc Ser 165	Glu	Ser	Leu	Ser	His 170	Thr	Gly	Tyr	Thr	531
Asn 175	Lys	Trp	Phe	Phe	Val 180	acc Thr	Ile	Thr	Asn	Asn 185	Ile	Met	Gly	Tyr	Met 190	579
Lys	Leu	Tyr	Ile	Asn 195	Gly	gag Glu	Leu	Lys	Gln 200	Ser	Gln	Lys	Ile	Glu 205	Asp	627
Leu	Asp	Glu	Val 210	Lys	Leu	gac Asp	Lys	Thr 215	Ile	Val	Phe	Gly	Ile 220	Asp	Glu	675
						atg Met										723

					aac Asn											771
					atc Ile 260	-	_						-	_		819
_		_			atc Ile			_				_	_			867
_					gtc Val	_	_	_	_	_			_	_		915
					aac Asn											963
					atc Ile											1011
					aag Lys 340											1059
					ggt Gly											1107
Lys	Leu	Gln	Ser 370	Asn	ctg Leu	Gly	Asn	Tyr 375	Gly	Ile	Gly	Ile	Phe 380	Ser	Ile	1155
Lys	Asn	Ile 385	Val	Ser	aag Lys	Asn	Lys 390	Tyr	Cys	Ser	Gln	Ile 395	Phe	Ser	Ser	1203
Phe	Arg 400	Glu	Asn	Thr	atg Met	Leu 405	Leu	Ala	Asp	Ile	Tyr 410	Lys	Pro	Trp	Arg	1251
					gcc Ala 420											1299
acc Thr	aag Lys	ctg Leu	ctg Leu	tcc Ser 435	acc Thr	tcc Ser	tcc Ser	ttc Phe	tgg Trp 440	aag Lys	ttc Phe	atc Ile	tcc Ser	cgt Arg 445	gac Asp	1347
		tgg Trp	_		taat	agga	at t	c								1374

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370
                         375
                                             380
Ile Val Ser Lys Asn Lys Tyr Cys Ser Gln Ile Phe Ser Ser Phe Arg
                    390
                                         395
Glu Asn Thr Met Leu Leu Ala Asp Ile Tyr Lys Pro Trp Arg Phe Ser
                                     410
Phe Lys Asn Ala Tyr Thr Pro Val Ala Val Thr Asn Tyr Glu Thr Lys
                                 425
Leu Leu Ser Thr Ser Ser Phe Trp Lys Phe Ile Ser Arg Asp Pro Gly
        435
                             440
Trp Val Glu
    450
<210> 13
<211> 1400
<212> DNA
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<221> CDS
<222> (10)...(1356)
<400> 13
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          Met Gly Glu Ser Gln Gln Glu Leu Asn Ser Met Val Thr Asp
acc cta aat aat agt att cct ttt aag ctt tct tct tat aca gat gat
                                                                   99
Thr Leu Asn Asn Ser Ile Pro Phe Lys Leu Ser Ser Tyr Thr Asp Asp
 15
aaa att tta att tcc tac ttc aac aag ttc ttc aag aga att aag tct
                                                                   147
Lys Ile Leu Ile Ser Tyr Phe Asn Lys Phe Phe Lys Arg Ile Lys Ser
tet tee gtt tta aac atg aga tae aag aat gat aaa tae gte gae act
                                                                   195
Ser Ser Val Leu Asn Met Arg Tyr Lys Asn Asp Lys Tyr Val Asp Thr
tcc ggt tac gac tcc aat atc aac att aac ggt gac gtg tac aag tac
                                                                   243
Ser Gly Tyr Asp Ser Asn Ile Asn Ile Asn Gly Asp Val Tyr Lys Tyr
         65
                             70
cca act aac aaa aac caa ttc ggt atc tac aac gac aag ctt act gaq
                                                                   291
Pro Thr Asn Lys Asn Gln Phe Gly Ile Tyr Asn Asp Lys Leu Thr Glu
     80
                         85
ctg aac atc tct caa aac gac tac att atc tac gac aac aag tac aag
Leu Asn Ile Ser Gln Asn Asp Tyr Ile Ile Tyr Asp Asn Lys Tyr Lys
95
                    100
aac ttc tct att tct ttc tgg gtc agg att cct aac tac gac aac aag
Asn Phe Ser Ile Ser Phe Trp Val Arg Ile Pro Asn Tyr Asp Asn Lys
                                     120
```

	gtc Val											_	_	_	_	435
	aac Asn				-	-										483
	ttg Leu 160		_		-					_		-				531
	aac Asn															579
	atc Ile															627
	tta Leu															675
	gac Asp															723
	ggc Gly 240															771
	att Ile															819
gac Asp	ttc Phe	tgg Trp	ggt Gly	aac Asn 275	tac Tyr	ttg Leu	ctt Leu	tac Tyr	gac Asp 280	aag Lys	gaa Glu	tac Tyr	tac Tyr	tta Leu 285	tta Leu	867
	gtg Val															915
tta Leu	agc Ser	att Ile 305	aac Asn	aac Asn	atc Ile	aga Arg	agc Ser 310	act Thr	att Ile	ctt Leu	tta Leu	gct Ala 315	aac Asn	aga Arg	tta Leu	963
tac Tyr	tct Ser 320	ggt Gly	atc Ile	aag Lys	gtt Val	aag Lys 325	atc Ile	caa Gln	aga Arg	gtt Val	aac Asn 330	aac Asn	tct Ser	tct Ser	act Thr	1011
	gat Asp			Val												1059
gct	agc	aag	act	cac	tta	ttc	сса	tta	tat	gct	gat	acc	gct	acc	acc	1107

	Lys	Thr	His 355	Leu	Phe	Pro	Leu	Tyr 360	Ala	Asp	Thr	Ala	Thr 365	Thr	
aac aag Asn Lys															1155
caa gto Gln Val	_	_	_			_				_		_			1203
aaa aat Lys Asr 400	Asn														1251
act gta Thr Val 415															1299
aac ago Asn Ser															1347
caa gaa Gln Glu		taat	aggg	gat o	cgcg	gccg	gc ac	gcgt	cccg	gga	actag	gtga			1396
attc															1400
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	LCILI	ıcıal		-											
<220> <223> E		ed po	olype			as	synth	ietio	c cor	ıstrı	ıct l	oased	ì		
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<220> <223> E	ncode n Bol	ed po	olype Ic	eptic	l e of									Leu	
<220> <223> E	ncode n Bol 4 Glu	ed po NTE H Ser	olype Ic Gln 5	eptió Gln	le of Glu	Leu	Asn	Ser 10	Met	Val	Thr	Asp	Thr 15		
<220> <223> E	ncode n Bol 4 Glu Ser	ed po NTE H Ser Ile 20	olype Hc Gln 5 Pro	Gln Phe	le of Glu Lys	Leu Leu	Asn Ser 25	Ser 10 Ser	Met Tyr	Val Thr	Thr Asp Lys	Asp Asp 30	Thr 15 Lys	Ile	
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<220> <223> E <400> 1 Met Gly 1 Asn Asn Leu Ile Val Leu 50 Tyr Asp 65 Asn Lys Ile Ser	ncode n BoN 4 Glu Ser Ser 35 Asn Ser Asn Gln Ser 115	ed po NTE H Ser Ile 20 Tyr Met Asn Gln Asn 100 Phe	olype Hc Gln 5 Pro Phe Arg Ile Phe 85 Asp	Gln Phe Asn Tyr Asn 70 Gly Tyr	Glu Lys Lys 55 Ile Ile Ile Arg	Leu Leu Phe 40 Asn Tyr Ile Ile 120	Asn Ser 25 Phe Asp Gly Asn Tyr 105 Pro	Ser 10 Ser Lys Lys Asp Asp Asp	Met Tyr Arg Tyr Val 75 Lys Asn Tyr	Val Thr Ile Val 60 Tyr Leu Lys Asp	Thr Asp Lys 45 Asp Lys Thr Tyr Asn 125	Asp Asp 30 Ser Thr Tyr Glu Lys 110 Lys	Thr 15 Lys Ser Ser Pro Leu 95 Asn	Ile Ser Gly Thr 80 Asn Phe	

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Ser Gly Trp Lys Val Ser Leu Asn His Asn Glu Ile Ile Trp Thr Leu
145
                    150
                                         155
Gln Asp Asn Ala Gly Ile Asn Gln Lys Leu Ala Phe Asn Tyr Gly Asn
                                    170
Ala Asn Gly Ile Ser Asp Tyr Ile Asn Lys Trp Ile Phe Val Thr Ile
            180
                                185
Thr Asn Asp Arg Leu Gly Asp Ser Lys Leu Tyr Ile Asn Gly Asn Leu
                            200
Ile Asp Gln Lys Ser Ile Leu Asn Leu Gly Asn Ile His Val Ser Asp
                        215
                                             220
Asn Ile Leu Phe Lys Ile Val Asn Cys Ser Tyr Thr Arg Tyr Ile Gly
                    230
                                         235
Ile Arg Tyr Phe Asn Ile Phe Asp Lys Glu Leu Asp Glu Thr Glu Ile
                                    250
Gln Thr Leu Tyr Ser Asn Glu Pro Asn Thr Asn Ile Leu Lys Asp Phe
            260
                                265
Trp Gly Asn Tyr Leu Leu Tyr Asp Lys Glu Tyr Tyr Leu Leu Asn Val
                            280
                                                 285
Leu Lys Pro Asn Asn Phe Ile Asp Arg Arg Lys Asp Ser Thr Leu Ser
                        295
Ile Asn Asn Ile Arg Ser Thr Ile Leu Leu Ala Asn Arg Leu Tyr Ser
                    310
                                        315
Gly Ile Lys Val Lys Ile Gln Arg Val Asn Asn Ser Ser Thr Asn Asp
                                    330
Asn Leu Val Arg Lys Asn Asp Gln Val Tyr Ile Asn Phe Val Ala Ser
            340
                                345
Lys Thr His Leu Phe Pro Leu Tyr Ala Asp Thr Ala Thr Thr Asn Lys
                            360
Glu Lys Thr Ile Lys Ile Ser Ser Ser Gly Asn Arg Phe Asn Gln Val
    370
                        375
Val Val Met Asn Ser Val Gly Asn Asn Cys Thr Met Asn Phe Lys Asn
                    390
                                        395
Asn Asn Gly Asn Asn Ile Gly Leu Leu Gly Phe Lys Ala Asp Thr Val
                405
                                    410
Val Ala Ser Thr Trp Tyr Tyr Thr His Met Arg Asp His Thr Asn Ser
            420
                                425
Asn Gly Cys Phe Trp Asn Phe Ile Ser Glu Glu His Gly Trp Gln Glu
                            440
Lys
<210> 15
<211> 1317
<212> DNA
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Met Ser Tyr Thr Asn Asp Lys Ile Leu Ile Leu Tyr Phe Asn

<213> Artificial Sequence

<221> CDS

<400> 15

<222> (10)...(1305)

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<223> Synthetic construct based on BoNTA Hc

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											tcc Ser				147
		 _	_							_	aac Asn	_			195
			_				_			_	cag Gln 75			_	243
				-		-					tcc Ser			_	291
_		_				_	_		_		aac Asn				339
											aag Lys			_	387
					-		_	_	_		gcc Ala				435
							_	_			atc Ile 155		_		483
											cgt Arg				531
											aag Lys				579
											ttc Phe				627
											ttc Phe				675
											tac Tyr 235				723



		cca Pro														771
		cgt Arg			_	_		_	_	_		_	_			819
		aac Asn														867
		cca Pro														915
		atc Ile 305							_					_		963
		aga Arg														1011
		tac Tyr									_			_	_	1059
		aag Lys														1107
		gtc Val														1155
		aac Asn 385														1203
		gct Ala														1251
tcc Ser 415	aac Asn	ggt Gly	tgc Cys	ttc Phe	tgg Trp 420	tcc Ser	ttc Phe	atc Ile	tcc Ser	aag Lys 425	gag Glu	cac His	ggt Gly	tgg Trp	cag Gln 430	1299
gag Glu		taat	agga	at t	.c											1317

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<210> 16

<211> 432

<212> PRT

<213> Artificial Sequence

<220>

<223> Encoded polypeptide of a synthetic construct based on BoNTF Hc

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405 410 415 Gly Cys Phe Trp Ser Phe Ile Ser Lys Glu His Gly Trp Gln Glu Asn 420 425 <210> 17 <211> 1368 <212> DNA <213> Artificial Sequence <223> Synthetic construct based on BoNTA Hc <221> CDS <222> (10) ... (1356) <400> 17 gaattcacg atg aag gac acc atc ctg atc cag gtc ttc aac aac tac atc 51 Met Lys Asp Thr Ile Leu Ile Gln Val Phe Asn Asn Tyr Ile tcc aac atc tcc tcc aac gcc atc ctg tcc ctg tcc tac cgt ggt ggt 99 Ser Asn Ile Ser Ser Asn Ala Ile Leu Ser Leu Ser Tyr Arg Gly Gly 15 cgt ctg atc gac tcc tcc ggt tac gga gcc acc atg aac gtc ggt tcc Arg Leu Ile Asp Ser Ser Gly Tyr Gly Ala Thr Met Asn Val Gly Ser 45 gac gtc atc ttc aac gac atc ggt aac ggt cag ttc aag ctg aac aac 195 Asp Val Ile Phe Asn Asp Ile Gly Asn Gly Gln Phe Lys Leu Asn Asn tcc gag aac tcc aac atc acc gcc cac cag tcc aag ttc gtc gtc tac 243 Ser Glu Asn Ser Asn Ile Thr Ala His Gln Ser Lys Phe Val Val Tyr gac tcc atg ttc gac aac ttc tcc atc aac ttc tgg gtc cgt acc cca 291 Asp Ser Met Phe Asp Asn Phe Ser Ile Asn Phe Trp Val Arg Thr Pro aag tac aac aac gac atc cag acc tac ctg cag aac gag tac acc 339 Lys Tyr Asn Asn Asn Asp Ile Gln Thr Tyr Leu Gln Asn Glu Tyr Thr 95 100 110

atc atc tcc tgt atc aag aac gac tcc ggt tgg aag gtc tcc atc aag Ile Ile Ser Cys Ile Lys Asn Asp Ser Gly Trp Lys Val Ser Ile Lys

gga aac cgt atc atc tgg acc ctg atc gac gtc aac gcc aag tcc aag Gly Asn Arg Ile Ile Trp Thr Leu Ile Asp Val Asn Ala Lys Ser Lys

tcc atc ttc ttc gag tac tcc atc aag gac aac atc tcc gac tac atc

Ser Ile Phe Phe Glu Tyr Ser Ile Lys Asp Asn Ile Ser Asp Tyr Ile 145 150 155 483

115

130



					atc Ile					_	_	_			_	531
					ggt Gly 180											579
_	_	_			tcc Ser			_		_		_	_			627
					aag Lys		_			_	_					675
			_		gcc Ala		_	_			_				_	723
					ctg Leu											771
					ctg Leu 260											819
					gcc Ala			Gly								867
					atc Ile											915
					gcc Ala											963
					gac Asp											1011
					gtc Val 340											1059
					gcc Ala											1107
					aag Lys											1155
atc	ctg	tgc	gag	aag	gac	acc	aag	acc	ttc	gga	ctg	ttc	ggt	atc	ggt	1203



Ile Leu Cys Glu Lys Asp Thr Lys Thr Phe Gly Leu Phe Gly Ile Gly 390 aag tto gto aag gao tac ggt tac gto tgg gao aco tac gao aac tac 1251 Lys Phe Val Lys Asp Tyr Gly Tyr Val Trp Asp Thr Tyr Asp Asn Tyr 400 tto tgt ato too cag tgg tac ctg cgt cgt ato too gag aac ato aac 1299 Phe Cys Ile Ser Gln Trp Tyr Leu Arg Arg Ile Ser Glu Asn Ile Asn 420 aag ctg cgt ctg gga tgt aac tgg cag ttc atc cca gtc gac gaq qqt 1347 Lys Leu Arg Leu Gly Cys Asn Trp Gln Phe Ile Pro Val Asp Glu Gly 435 440 tgg acc gag taataggaat tc 1368 Trp Thr Glu <210> 18 <211> 449 <212> PRT <213> Artificial Sequence <220> <223> Encoded polypeptide of a synthetic construct based on BoNTG Hc <400> 18 Met Lys Asp Thr Ile Leu Ile Gln Val Phe Asn Asn Tyr Ile Ser Asn 10 Ile Ser Ser Asn Ala Ile Leu Ser Leu Ser Tyr Arg Gly Gly Arg Leu 25 Ile Asp Ser Ser Gly Tyr Gly Ala Thr Met Asn Val Gly Ser Asp Val 40 4.5 Ile Phe Asn Asp Ile Gly Asn Gly Gln Phe Lys Leu Asn Asn Ser Glu Asn Ser Asn Ile Thr Ala His Gln Ser Lys Phe Val Val Tyr Asp Ser Met Phe Asp Asn Phe Ser Ile Asn Phe Trp Val Arg Thr Pro Lys Tyr 90 Asn Asn Asp Ile Gln Thr Tyr Leu Gln Asn Glu Tyr Thr Ile Ile 100 105 110 Ser Cys Ile Lys Asn Asp Ser Gly Trp Lys Val Ser Ile Lys Gly Asn 120 Arg Ile Ile Trp Thr Leu Ile Asp Val Asn Ala Lys Ser Lys Ser Ile 135 Phe Phe Glu Tyr Ser Ile Lys Asp Asn Ile Ser Asp Tyr Ile Asn Lys 150 155 Trp Phe Ser Ile Thr Ile Thr Asn Asp Arg Leu Gly Asn Ala Asn Ile 165 170 Tyr Ile Asn Gly Ser Leu Lys Lys Ser Glu Lys Ile Leu Asn Leu Asp 185 Arg Ile Asn Ser Ser Asn Asp Ile Asp Phe Lys Leu Ile Asn Cys Thr 200

Asp Thr Thr Lys Phe Val Trp Ile Lys Asp Phe Asn Ile Phe Gly Arg

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Glu Leu Asn Ala Thr Glu Val Ser Ser Leu Tyr Trp Ile Gln Ser Ser
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Thr Asn Thr Leu Lys Asp Phe Trp Gly Asn Pro Leu Arg Tyr Asp Thr
                                     250
Gln Tyr Tyr Leu Phe Asn Gln Gly Met Gln Asn Ile Tyr Ile Lys Tyr
            260
                                 265
Phe Ser Lys Ala Ser Met Gly Glu Thr Ala Pro Arg Thr Asn Phe Asn
                             280
                                                 285
Asn Ala Ala Ile Asn Tyr Gln Asn Leu Tyr Leu Gly Leu Arg Phe Ile
                        295
                                             300
Ile Lys Lys Ala Ser Asn Ser Arg Asn Ile Asn Asn Asp Asn Ile Val
                    310
                                         315
Arg Glu Gly Asp Tyr Ile Tyr Leu Asn Ile Asp Asn Ile Ser Asp Glu
                                     330
Ser Tyr Arg Val Tyr Val Leu Val Asn Ser Lys Glu Ile Gln Thr Gln
            340
                                 345
Leu Phe Leu Ala Pro Ile Asn Asp Asp Pro Thr Phe Tyr Asp Val Leu
                             360
Gln Ile Lys Lys Tyr Tyr Glu Lys Thr Thr Tyr Asn Cys Gln Ile Leu
                        375
Cys Glu Lys Asp Thr Lys Thr Phe Gly Leu Phe Gly Ile Gly Lys Phe
                    390
                                         395
Val Lys Asp Tyr Gly Tyr Val Trp Asp Thr Tyr Asp Asn Tyr Phe Cys
                405
                                     410
Ile Ser Gln Trp Tyr Leu Arg Arg Ile Ser Glu Asn Ile Asn Lys Leu
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                                 425
Arg Leu Gly Cys Asn Trp Gln Phe Ile Pro Val Asp Glu Gly Trp Thr
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Glu
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<211> 1242
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1
tto too cog tot gaa gac aac tto act aac gac ctg aac aaa ggc qaa
                                                                   96
Phe Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu
             20
gaa atc acc tcc gac act aac atc gaa gct gct gaa gaa aac atc tct
Glu Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser
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_	_	_		_	cag Gln			_					_		_	192
					atc Ile 70										cag , Gln 80	240
					aac Asn											288
					acc Thr	_				_	_	_	_	_		336
					cgt Arg		_	_				_		_	_	384
					cgc Arg											432
					gct Ala 150		_	_	-	_		_			_	480
					gac Asp											528
					gac Asp											576
					aac Asn											624
					gct Ala											672
					ggt Gly 230											720
					cag Gln											768
					gtt Val											816
aaa	gtt	aac	act	cag	atc	gac	ctg	atc	cgt	aag	aag	atg	aaa	gaa	gct	864

Lys	Val	Asn 275	Thr	Gln	Ile	Asp	Leu 280	Ile	Arg	Lys	Lys	Met 285	Lys	Glu	Ala	
	gaa Glu 290			-	_	_			_					_		912
	cag Gln			_	_	_	_								_	960
	ctg Leu															1008
	aac Asn			_		_	_		-			_	_			1056
	atc Ile															1104
	gac Asp 370															1152
	cag Gln															1200
	atc Ile												taa	٠		1242
<211 <211 <211 <221	3 > Er	.3 RT rtifi	d pc	olype			ā a s	syntl	netio	e cor	ıstru	ıct b	oased	ı		
)> 20															
1	Ala			5					10			_	_	15		
	Ser		20					25					30			
	Ile	35					40					45				
	Asp 50					55					60					
65	Glu				70					75					80	
Leu	Glu	Leu	Met	Pro	Asn	Ile	Glu	Arg	Phe	Pro	Asn	Gly	Lys	Lys	Tyr	

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85
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Glu His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala
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Leu Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val
                        135
Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val
                    150
                                        155
Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr
                                    170
Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Ile Pro Tyr Ile Gly Pro
            180
                                 185
Ala Leu Asn Ile Gly Asn Met Leu Tyr Lys Asp Asp Phe Val Gly Ala
                            200
Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile
                        215
Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn
                    230
                                        235
Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn
                                    250
Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala
            260
                                265
Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala
                            280
Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr
                        295
Asn Gln Tyr Thr Glu Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp
                    310
                                        315
Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn
                325
                                    330
Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser
                                345
Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu
                            360
Lys Asp Ala Leu Leu Lys Tyr Ile Arg Asp Asn Tyr Gly Thr Leu Ile
                        375
                                            380
Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr
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<211> 1242
<212> DNA
<213> Artificial Sequence
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<220>

<223> Synthetic construct based on BoNTA Hc

<221> CDS

<222> (1)...(1239)

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																96
					_							_				144
																192
																240
																288
																336
																384
																432
																480
																528
atc Ile	tcc Ser	ttg Leu	att Ile 180	gtc Val	cca Pro	tac Tyr	atc Ile	ggt Gly 185	ttg Leu	gcc Ala	ttg Leu	aac Asn	gtc Val 190	ggt Gly	aac Asn	576
gag Glu	acc Thr	gcc Ala 195	aag Lys	ggt Gly	aac Asn	ttc Phe	gag Glu 200	aac Asn	gct Ala	ttc Phe	gag Glu	atc Ile 205	gct Ala	ggt Gly	gcc Ala	624
tcc Ser	atc Ile 210	ttg Leu	ttg Leu	gag Glu	ttc Phe	atc Ile 215	cca Pro	gag Glu	ttg Leu	ttg Leu	atc Ile 220	cca Pro	gtc Val	gtc Val	ggt Gly	672
gcc Ala 225	ttc Phe	ttg Leu	ttg Leu	gag Glu	tcc Ser 230	tac Tyr	atc Ile	gac Asp	aac Asn	aag Lys 235	aac Asn	aag Lys	atc Ile	atc Ile	aag Lys 240	720
	atc Ile atc Ile aach to the atc Ile at	Ile Ala atc gag Ile Glu aac gag Ser Glu tcc gag Tyr Glu atc tcc Ile Phe atc tcc Ile Ser gtc tac Val Tyr 130 gtc gag Val Glu ttc gtc Phe Val atc tcc Ile Ser gag acc Glu Thr tcc atc Ser atc Ser gag acc Glu Thr	Ile Ala Asp atc gag tac Ile Glu Tyr 35 aac gag ttg Asn Glu Leu 50 tcc gag aac Eser Glu Asn 65 tac gag tac Ile Clu Ile	Ile Ala Asp Lys 20 atc gag tac Asn 35 aac gag ttg atc Ile 500 tcc gag aac acc Thr 65 tac gag aag caa Tyr gloo atc tcc Leu Thr 100 atc tcc Leu Thr 115 gtc tac tcc ttg Tyr 100 gtc gag gcc ttc tg atc Ile Ser Leu Thr 115 ttc gtc tac tcc ttc the 130 gtc gag gcc ttc ttg att gag he leu Leu Leu Ile 180 gag acc ttc ttg Leu Leu Ile 180 gag ttc ttg ttg Leu Leu Ile 180 gag acc ttc ttg Leu Leu Ile 180 gcc atc ttg ttg Leu Leu Ile	Ile Ala Asp Lys Asn atc gag tac aac Thr aac gag ttg atc ttg Asn Glu Leu Ile Leu tcc gag aac acc gag ser Glu Asn Thr Glu tac gag aag caa cca Ile Phe Gln Tyr Leu atc tcc ttg acc tct Ile Ser Leu Thr Ser gtc gag gcc phe Phe Val Ala Gly Leu ttc gtc atc gag gct Yal ale gag gct ttg Val ale gag gct gg ttc gag gcc gag gct Ile ser Leu lae gag gag acc gcc aag ggt tcc atc ttg ttg gag du leu leu gag du leu gag gag du leu leu gag	Ile Ala Asp Lys Asn Ser atc gag tac aac acc cag Asn Glu Leu Ile Leu Asp 50 Leu Ile Leu Asp ser Glu Leu Ile Leu Asp ser Glu Asn Thr Glu Ser Tyr Glu Lys Gln Pro Ala atc ttc Caa tac tcc Tyr atc tcc ttg Thr Ser Ser Ile Ser Leu Thr Ser Ser gtc tac ttc ttc ttc tcc Yal Glu Ala Gly Leu Phe 130 Thr Ser Phe Phe Ser gtc gag gcc ggt ttc Phe 130 Thr Ser Phe Phe Ser 9tc gag gcc ggt ttc Phe 150 Thr gag gcc ggt acc 165 Thr gag ggt acc 165 Thr Ala Lys Gly Asn 165 Th	The Ala Asp Lys Asm Ser Phe 20 Asm Ser Cag Ser Ser Phe 20 atc Ile Glu Tyr Asm Thr Gln Ser 35 teg Tyr Asm Thr Gln Ser Thr 55 aac gag ttg Leu Ile Leu Asp 55 teg gag tcc ttg Ser Glu Asm Thr Glu Ser Thr 70 tcc gag aac aac acc gag tcc ttg Ser Glu Lys Gln Pro Ala Ile 85 teu Tyr Ser Leu Tyr Ser Ala Ile 85 atc ttc ttg Leu Tyr 100 tet ttc Tyr Ser Ser Phe 115 gtc tac ttg Tyr 100 tet ttc ttc ttg Tyr Ser Ser Phe 130 gtc Yal Tyr 130 get ttg ttg ttg ttc get Ala 150 gtc Yal Glu Ala Gly Leu Phe Ala 150 Ala Ile Glu Ala Asm Lys 165 atc tcc ttg Lug Ala Asm Lys 165 Tyr 180 gtc Ser Leu Ile Glu Ala Asm Lys 165 Tyr 180 gag acc Lug Lug Blu Lug Cal Asm Lys 165 Tyr 180 atc tcc ttg Lug Blu Lug Cal Asm Lys 165 Tyr 180 gag acc Lug Lug Blu Lug Cal Asm Lys 165 Tyr 180 gag acc Lug Lug Blu Lug Cal Asm Lys 165 Tyr 180 gag acc Lug Lug Blu Lug Cal Asm Lys 165 Tyr 180 gag acc Lug Lug Blu Lug Cal Asm Lys 165 Tyr 180 gag acc Lug Cal Asm Lys 165 Tyr 180 gag acc Lug Cal Asm Lys 165 Tyr 180 atc Lug Cal Asm Lys 165 Tyr 180	Ile Ala Asp Lys 20 Asn Ser Phe Ser atc gag tac 35 aac Asn acc Thr cag Gln tcc Asn Asn aac Asn gag Glu teu Ile teu Asp Fo Asn tcc Ser Asn gag Asn tcc Thr To gac Asp Thr tcc Asp Thr gac Asp Thr tcc Asp Thr gac Asp Thr tcc Asp Thr tcc Thr tcc Asp Thr tcc Thr tcc Asp Thr tcc Thr tcc Thr tcc Thr tcc Thr <	Ile Ala Asp 20 Asn 3ch 20 Ser Phe 25 Ser Asp 25 atc 3ch 2ch 2ch 2ch 2ch 2ch 2ch 2ch 2ch 2ch 2	Ile Ala Asp Lys 20 Asn Ser Phe Ser Asp 25 Asp 25 <th< td=""><td>Ile Ala Asp gag Lys 20 Asn sor 20 Phe ser 25 Asp 25 Asp 26 Leu 25 atc 31e gag tac 35 asc 35<!--</td--><td>The Ala Asp Lys 20 Lys 20 Ser Phe Ser Asp Asp Asp Leu Ser 25 Asp Asp Asp Leu Ser 25 Asp Asp Asp Asp Asp Asp Asp Asp Asp Asp</td><td>The Ala Asp Lys 20 Asp 20</td><td>The Ala Asp Say Lys 20 Asn Ser Phe Ser Asp Asp Asp Asp Leu Ser Lys Asn 30 Ser Say Asp 25 Asn Say Asp 25 Leu Ser Lys Asn 30 Asn 30 atc gag tac aac aac acc Sile Say Asp 35 Ser Say Asp 35 Ser Say Say Say Say Say Say Say Say Say Say</td><td> The Ala Asp Lys Asn Ser Phe Ser Asp Asp Leu Ser Lys Asn Glu Car </td><td>atc gag tac aac acc cag tcc aac tac atc gag aac gac ttc cca atc atc gag atc gag ttg cca atc and atc atc gag atc gag ttg cca atc and atc atc gag atc gag ttg cca atc and atc atc gag atc gag ttg cca as and atc gag atc gag atc gac gtc gac gtc cca gtc gac gag aac acc gag tcc gag atc gac gtc gac gtc cca gtc gag aac acc gag tcc gag atc gag at</td></td></th<>	Ile Ala Asp gag Lys 20 Asn sor 20 Phe ser 25 Asp 25 Asp 26 Leu 25 atc 31e gag tac 35 asc 35 </td <td>The Ala Asp Lys 20 Lys 20 Ser Phe Ser Asp Asp Asp Leu Ser 25 Asp Asp Asp Leu Ser 25 Asp Asp Asp Asp Asp Asp Asp Asp Asp Asp</td> <td>The Ala Asp Lys 20 Asp 20</td> <td>The Ala Asp Say Lys 20 Asn Ser Phe Ser Asp Asp Asp Asp Leu Ser Lys Asn 30 Ser Say Asp 25 Asn Say Asp 25 Leu Ser Lys Asn 30 Asn 30 atc gag tac aac aac acc Sile Say Asp 35 Ser Say Asp 35 Ser Say Say Say Say Say Say Say Say Say Say</td> <td> The Ala Asp Lys Asn Ser Phe Ser Asp Asp Leu Ser Lys Asn Glu Car </td> <td>atc gag tac aac acc cag tcc aac tac atc gag aac gac ttc cca atc atc gag atc gag ttg cca atc and atc atc gag atc gag ttg cca atc and atc atc gag atc gag ttg cca atc and atc atc gag atc gag ttg cca as and atc gag atc gag atc gac gtc gac gtc cca gtc gac gag aac acc gag tcc gag atc gac gtc gac gtc cca gtc gag aac acc gag tcc gag atc gag at</td>	The Ala Asp Lys 20 Lys 20 Ser Phe Ser Asp Asp Asp Leu Ser 25 Asp Asp Asp Leu Ser 25 Asp	The Ala Asp Lys 20 Asp 20	The Ala Asp Say Lys 20 Asn Ser Phe Ser Asp Asp Asp Asp Leu Ser Lys Asn 30 Ser Say Asp 25 Asn Say Asp 25 Leu Ser Lys Asn 30 Asn 30 atc gag tac aac aac acc Sile Say Asp 35 Ser Say Asp 35 Ser Say	The Ala Asp Lys Asn Ser Phe Ser Asp Asp Leu Ser Lys Asn Glu Car	atc gag tac aac acc cag tcc aac tac atc gag aac gac ttc cca atc atc gag atc gag ttg cca atc and atc atc gag atc gag ttg cca atc and atc atc gag atc gag ttg cca atc and atc atc gag atc gag ttg cca as and atc gag atc gag atc gac gtc gac gtc cca gtc gac gag aac acc gag tcc gag atc gac gtc gac gtc cca gtc gag aac acc gag tcc gag atc gag at

				_	_		_	_			_	tgg Trp		_	_	768
								_			_	aac Asn				816
			_			_		_	_	_		tac Tyr 285	_	_		864
_	_					_		_				tac Tyr			_	912
							_			_		aac Asn		_	_	960
						_		_				aac Asn				1008
												cca Pro				1056
												aac Asn 365				1104
												gct Ala				1152
		Lys	Val	Asn		Tyr	Leu	Lys	Thr	Ile	Met	cca Pro		Asp		1200
tcc Ser	atc Ile	tac Tyr	acc Thr	aac Asn 405	gac Asp	acc Thr	atc Ile	ttg Leu	atc Ile 410	gag Glu	atg Met	ttc Phe	taa			1242
<210)> 22															

<211> 413

<212> PRT

<213> Artificial Sequence

<220>

<223> Encoded polypeptide of a synthetic construct based on BoNTB Hn

<400> 22

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<210> 23

<211> 1200

<212> DNA

<213> Artificial Sequence

<220> <223> Synthetic construct based on BoNTA Hc <221> CDS <222> (1) . . . (1197) <400> 23 atg tcc ctg tac aac aag acc ctt gac tgt aga gag ctg ctg gtg aag 48 Met Ser Leu Tyr Asn Lys Thr Leu Asp Cys Arg Glu Leu Leu Val Lys aac act gac ctg cca ttc atc ggt gac atc agt gac gtg aag act gac Asn Thr Asp Leu Pro Phe Ile Gly Asp Ile Ser Asp Val Lys Thr Asp atc ttc ctg cgt aag gac atc aac gag gag act gag gtg atc tac tac Ile Phe Leu Arg Lys Asp Ile Asn Glu Glu Thr Glu Val Ile Tyr Tyr cca gac aac gtg tca gta gac caa gtg atc ctc agt aag aac acc tcc 192 Pro Asp Asn Val Ser Val Asp Gln Val Ile Leu Ser Lys Asn Thr Ser gag cat gga caa cta gac ctg ctc tac cct agt atc gac agt gag agt 240 Glu His Gly Gln Leu Asp Leu Leu Tyr Pro Ser Ile Asp Ser Glu Ser gag atc ctg cca ggg gag aat caa gtc ttc tac gac aac cgt acc cag 288 Glu Ile Leu Pro Gly Glu Asn Gln Val Phe Tyr Asp Asn Arg Thr Gln 85 aac gtg gac tac ctg aac tcc tac tac tac cta qaq tct caq aaq ctq 336 Asn Val Asp Tyr Leu Asn Ser Tyr Tyr Tyr Leu Glu Ser Gln Lys Leu 100 agt gac aac gtg gag gac ttc act ttc acg cgt tca atc gag gag gct 384 Ser Asp Asn Val Glu Asp Phe Thr Phe Thr Arg Ser Ile Glu Glu Ala 115 120 125 ctg gac aac agt gca aag gtg tac act tac ttc cct acc ctg gct aac 432 Leu Asp Asn Ser Ala Lys Val Tyr Thr Tyr Phe Pro Thr Leu Ala Asn 130 135 aag gtg aat gcc ggt gtg caa ggt ggt ctg ttc ctg atg tgg gca aac 480 Lys Val Asn Ala Gly Val Gln Gly Gly Leu Phe Leu Met Trp Ala Asn 150 gac gtg gtt gag gac ttc act acc aac atc ctg cgt aag gac aca ctg 528 Asp Val Val Glu Asp Phe Thr Thr Asn Ile Leu Arg Lys Asp Thr Leu 165 170 gac aag atc tca gat gtg tca gct atc atc ccc tac atc gga ccc gca 576 Asp Lys Ile Ser Asp Val Ser Ala Ile Ile Pro Tyr Ile Gly Pro Ala 180 185 ctg aac atc tcc aac tct gtg cgt cgt gga aac ttc act gag gca ttc

624



	Leu	Asn	Ile 195	Ser	Asn	Ser	Val	Arg 200	Arg	Gly	Asn	Phe	Thr 205	Glu	Ala	Phe	
						acc Thr											672
						gca Ala 230					_	_	_	_		_	720
						acc Thr											768
						tac Tyr											816
						aac Asn					_	_		_		_	864
						gca Ala		_	_	_		_	_			_	912
)						gac Asp 310											960
						gac Asp											1008
						gag Glu											1056
	ctg Leu	cct Pro	aag Lys 355	gtc Val	atc Ile	gac Asp	gag Glu	ctg Leu 360	aac Asn	gag Glu	ttc Phe	gac Asp	cga Arg 365	aac Asn	acc Thr	aag Lys	1104
						ctg Leu											1152
	gag Glu 385	gtc Val	gac Asp	aag Lys	ctg Leu	aag Lys 390	gca Ala	aag Lys	gta Val	aac Asn	aac Asn 395	agc Ser	ttc Phe	cag Gln	aac Asn		1197
	taa																1200
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<212> PRT

<213> Artificial Sequence

<220>

<223> Encoded polypeptide of a synthetic construct based on BoNTC Hn

<400> 24 Met Ser Leu Tyr Asn Lys Thr Leu Asp Cys Arg Glu Leu Leu Val Lys 10 Asn Thr Asp Leu Pro Phe Ile Gly Asp Ile Ser Asp Val Lys Thr Asp 20 25 Ile Phe Leu Arg Lys Asp Ile Asn Glu Glu Thr Glu Val Ile Tyr Tyr Pro Asp Asn Val Ser Val Asp Gln Val Ile Leu Ser Lys Asn Thr Ser Glu His Gly Gln Leu Asp Leu Leu Tyr Pro Ser Ile Asp Ser Glu Ser 75 Glu Ile Leu Pro Gly Glu Asn Gln Val Phe Tyr Asp Asn Arg Thr Gln 90 Asn Val Asp Tyr Leu Asn Ser Tyr Tyr Tyr Leu Glu Ser Gln Lys Leu 105 Ser Asp Asn Val Glu Asp Phe Thr Phe Thr Arg Ser Ile Glu Glu Ala 120 125 Leu Asp Asn Ser Ala Lys Val Tyr Thr Tyr Phe Pro Thr Leu Ala Asn 135 Lys Val Asn Ala Gly Val Gln Gly Gly Leu Phe Leu Met Trp Ala Asn 150 155 Asp Val Val Glu Asp Phe Thr Thr Asn Ile Leu Arg Lys Asp Thr Leu 170 Asp Lys Ile Ser Asp Val Ser Ala Ile Ile Pro Tyr Ile Gly Pro Ala 180 185 Leu Asn Ile Ser Asn Ser Val Arg Arg Gly Asn Phe Thr Glu Ala Phe 200 205 Ala Val Thr Gly Val Thr Ile Leu Leu Glu Ala Phe Pro Glu Phe Thr 215 Ile Pro Ala Leu Gly Ala Phe Val Ile Tyr Ser Lys Val Gln Glu Arg 230 235 Asn Glu Ile Ile Lys Thr Ile Asp Asn Cys Leu Glu Gln Arg Ile Lys 250 Arg Trp Lys Asp Ser Tyr Glu Trp Met Met Gly Thr Trp Leu Ser Arg 265 Ile Ile Thr Gln Phe Asn Asn Ile Ser Tyr Gln Met Tyr Asp Ser Leu 280 Asn Tyr Gln Ala Gly Ala Ile Lys Ala Lys Ile Asp Leu Glu Tyr Lys 295 300 Lys Tyr Ser Gly Ser Asp Lys Glu Asn Ile Lys Ser Gln Val Glu Asn 310 315 Leu Lys Asn Ser Leu Asp Val Lys Ile Ser Glu Ala Met Asn Asn Ile 330 Asn Lys Phe Ile Arg Glu Cys Ser Val Thr Tyr Leu Phe Lys Asn Met 340 345 Leu Pro Lys Val Ile Asp Glu Leu Asn Glu Phe Asp Arg Asn Thr Lys 360 Ala Lys Leu Ile Asn Leu Ile Asp Ser His Asn Ile Ile Leu Val Gly 375 Glu Val Asp Lys Leu Lys Ala Lys Val Asn Asn Ser Phe Gln Asn



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<210> 25
<211> 1161
<212> DNA
<213> Artificial Sequence
<223> Synthetic construct based on BoNTA Hc
<221> CDS
<222> (1) ... (1158)
<400> 25
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                                                                   48
Met Ala Asn Ser Arg Asp Asp Ser Thr Cys Ile Lys Val Lys Asn Asn
aga ctg cca tac gtt gcc gac aag gac tcc atc tcc cag gag atc ttc
                                                                   96
Arg Leu Pro Tyr Val Ala Asp Lys Asp Ser Ile Ser Gln Glu Ile Phe
             20
                                  25
gag aac aag atc atc acc gac gag acc aac gtt caa aac tac tcc gac
                                                                   144
Glu Asn Lys Ile Ile Thr Asp Glu Thr Asn Val Gln Asn Tyr Ser Asp
         35
aag tto tot ttg gac gag too ato otg gac ggt cag gto oca ato aac
                                                                   192
Lys Phe Ser Leu Asp Glu Ser Ile Leu Asp Gly Gln Val Pro Ile Asn
     50
cca gag atc gtc gac cca ctg ttg cca aac gtc aac atg gag cca ttg
                                                                   240
Pro Glu Ile Val Asp Pro Leu Leu Pro Asn Val Asn Met Glu Pro Leu
                     70
aac ttg cca ggt gag gag atc gtc ttc tac gac gac atc acc aag tac
                                                                   288
Asn Leu Pro Gly Glu Glu Ile Val Phe Tyr Asp Asp Ile Thr Lys Tyr
gtc gac tac ttg aac tcc tac tac ttg gag tct caa aag ttg tct
                                                                   336
Val Asp Tyr Leu Asn Ser Tyr Tyr Tyr Leu Glu Ser Gln Lys Leu Ser
            100
                                 105
aac aac gtc gag aac atc acc ttg acc acc tcc gtc gag gag gcc ttg
                                                                   384
Asn Asn Val Glu Asn Ile Thr Leu Thr Thr Ser Val Glu Glu Ala Leu
        115
                            120
ggt tac tct aac aag atc tac acc ttc ctg cca tcc ttg gct gag aag
Gly Tyr Ser Asn Lys Ile Tyr Thr Phe Leu Pro Ser Leu Ala Glu Lys
    130
                        135
gtt aac aag ggt gtt caa gct ggt ttg ttc ctg aac tgg gcc aac gag
                                                                   480
Val Asn Lys Gly Val Gln Ala Gly Leu Phe Leu Asn Trp Ala Asn Glu
145
                    150
gtc gtc gag gac ttc acc acc atc atg aag aag gac acc ctg gac
                                                                   528
Val Val Glu Asp Phe Thr Thr Asn Ile Met Lys Lys Asp Thr Leu Asp
                165
                                    170
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			_	_	tcc Ser	_				_	_	576
					gcc Ala							624
					ttc Phe							672
					ttc Phe 230							720
					atc Ile							768
					cag Gln				 _	_		816
					cac His							864
					atc Ile							912
					aag Lys 310							960
					gtc Val							1008
					tgt Cys							1056
					gag Glu		Lys					1104
					atc Ile							1152
gtt Val 385	gac Asp	taa										1161



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<210> 26
<211> 386
<212> PRT
<213> Artificial Sequence
<220>
<223> Encoded polypeptide of a synthetic construct based
      on BoNTD Hn
<400> 26
Met Ala Asn Ser Arg Asp Asp Ser Thr Cys Ile Lys Val Lys Asn Asn
Arg Leu Pro Tyr Val Ala Asp Lys Asp Ser Ile Ser Gln Glu Ile Phe
Glu Asn Lys Ile Ile Thr Asp Glu Thr Asn Val Gln Asn Tyr Ser Asp
                            40
Lys Phe Ser Leu Asp Glu Ser Ile Leu Asp Gly Gln Val Pro Ile Asn
                        55
Pro Glu Ile Val Asp Pro Leu Leu Pro Asn Val Asn Met Glu Pro Leu
                    70
                                        75
Asn Leu Pro Gly Glu Glu Ile Val Phe Tyr Asp Asp Ile Thr Lys Tyr
                                    90
Val Asp Tyr Leu Asn Ser Tyr Tyr Tyr Leu Glu Ser Gln Lys Leu Ser
                                105
Asn Asn Val Glu Asn Ile Thr Leu Thr Thr Ser Val Glu Glu Ala Leu
                            120
Gly Tyr Ser Asn Lys Ile Tyr Thr Phe Leu Pro Ser Leu Ala Glu Lys
                        135
Val Asn Lys Gly Val Gln Ala Gly Leu Phe Leu Asn Trp Ala Asn Glu
                    150
                                        155
Val Val Glu Asp Phe Thr Thr Asn Ile Met Lys Lys Asp Thr Leu Asp
                165
                                    170
Lys Ile Ser Asp Val Ser Val Ile Ile Pro Tyr Ile Gly Pro Ala Leu
                                185
Asn Ile Gly Asn Ser Ala Leu Arg Gly Asn Phe Asn Gln Ala Phe Ala
                            200
                                                205
Thr Ala Gly Val Ala Phe Leu Leu Glu Gly Phe Pro Glu Phe Thr Ile
                        215
                                            220
Pro Ala Leu Gly Val Phe Thr Phe Tyr Ser Ser Ile Gln Glu Arg Glu
                    230
                                        235
Lys Ile Ile Lys Thr Ile Glu Asn Cys Leu Glu Gln Arg Val Lys Arg
                                    250
Trp Lys Asp Ser Tyr Gln Trp Met Val Ser Asn Trp Leu Ser Arg Ile
            260
                                265
Thr Thr Gln Phe Asn His Ile Asn Tyr Gln Met Tyr Asp Ser Leu Ser
                            280
Tyr Gln Ala Asp Ala Ile Lys Ala Lys Ile Asp Leu Glu Tyr Lys Lys
                        295
Tyr Ser Gly Ser Asp Lys Glu Asn Ile Lys Ser Gln Val Glu Asn Leu
                    310
                                        315
Lys Asn Ser Leu Asp Val Lys Ile Ser Glu Ala Met Asn Asn Ile Asn
                325
                                    330
Lys Phe Ile Arg Glu Cys Ser Val Thr Tyr Leu Phe Lys Asn Met Leu
                                345
Pro Lys Val Ile Asp Glu Leu Asn Lys Phe Asp Leu Arg Thr Lys Thr
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Glu Leu Ile Asn Leu Ile Asp Ser His Asn Ile Ile Leu Val Gly Glu

370 375 380

Val Asp

<210> 27

<211> 1149

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic construct based on BoNTA Hc

<221> CDS

<222> (1) ... (1146)

<400> 27

atg tcc atc tgc atc gag atc aac aac ggt gag ctg ttc ttc gtg gct 48 Met Ser Ile Cys Ile Glu Ile Asn Asn Gly Glu Leu Phe Phe Val Ala

tcc gag aac agt tac aac gat gac aac atc aac act cct aag gag att 96 Ser Glu Asn Ser Tyr Asn Asp Asp Asn Ile Asn Thr Pro Lys Glu Ile 20 25 30

gac gac acc gtc act tct aac aac tac gaa aac gac ctg gac cag 144
Asp Asp Thr Val Thr Ser Asn Asn Asn Tyr Glu Asn Asp Leu Asp Gln
35 40 45

gtc atc cta aac ttc aac tcc gag tcc gcc cct ggt ctg tcc gac gag 192
Val Ile Leu Asn Phe Asn Ser Glu Ser Ala Pro Gly Leu Ser Asp Glu
50 55 60

aag ctg aac ctg acc atc cag aac gac gct tac atc cca aag tac gac 240 Lys Leu Asn Leu Thr Ile Gln Asn Asp Ala Tyr Ile Pro Lys Tyr Asp 65 70 75 80

tcc aac ggt aca tcc gat atc gag cat gac gtt aac gag ctt aac 288 Ser Asn Gly Thr Ser Asp Ile Glu Gln His Asp Val Asn Glu Leu Asn

gtc ttc ttc tac tta gac gct cag aag gtg ccc gag ggt gag aac aac 336
Val Phe Phe Tyr Leu Asp Ala Gln Lys Val Pro Glu Gly Glu Asn Asn
100 105 110

gtc aat ctc acc tct tca att gac aca gcc ttg ttg gag cag cct aag 384
Val Asn Leu Thr Ser Ser Ile Asp Thr Ala Leu Leu Glu Gln Pro Lys
115 120 125

atc tac acc ttc ttc tcc tcc gag ttc atc aac aac gtc aac aag cct 432
Ile Tyr Thr Phe Phe Ser Ser Glu Phe Ile Asn Asn Val Asn Lys Pro
130 135 140

gtg cag gcc gca ttg ttc gta agc tgg att cag cag gtg tta gta gac 480 Val Gln Ala Ala Leu Phe Val Ser Trp Ile Gln Gln Val Leu Val Asp 145 150 155 160



					_	aac Asn	_						_		_		528
				_	-	cca Pro				_	_	_					576
	_	-	_	_		aac Asn		_	_	-			_	_		_	624
						ttc Phe											672
						tcc Ser 230											720
						aac Asn											768
						ttc Phe											816
\						cga Arg											864
	cag Gln	gtc Val 290	aac Asn	gcc Ala	atc Ile	aag Lys	acc Thr 295	atc Ile	atc Ile	gag Glu	tcc Ser	aag Lys 300	tac Tyr	aac Asn	tcc Ser	tac Tyr	912
						aac Asn 310											960
						aac Asn											1008
						gag Glu											1056
						aac Asn											1104
						tac Tyr											1146

1149

taa

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<210> 28
<211> 382
<212> PRT
<213> Artificial Sequence
<223> Encoded polypeptide of a synthetic construct based
      on BoNTE Hn
<400> 28
Met Ser Ile Cys Ile Glu Ile Asn Asn Gly Glu Leu Phe Phe Val Ala
Ser Glu Asn Ser Tyr Asn Asp Asp Asn Ile Asn Thr Pro Lys Glu Ile
                                25
Asp Asp Thr Val Thr Ser Asn Asn Tyr Glu Asn Asp Leu Asp Gln
                            40
Val Ile Leu Asn Phe Asn Ser Glu Ser Ala Pro Gly Leu Ser Asp Glu
                        55
Lys Leu Asn Leu Thr Ile Gln Asn Asp Ala Tyr Ile Pro Lys Tyr Asp
                    70
                                        75
Ser Asn Gly Thr Ser Asp Ile Glu Gln His Asp Val Asn Glu Leu Asn
                85
                                    90
Val Phe Phe Tyr Leu Asp Ala Gln Lys Val Pro Glu Gly Glu Asn Asn
                                105
Val Asn Leu Thr Ser Ser Ile Asp Thr Ala Leu Leu Glu Gln Pro Lys
                            120
Ile Tyr Thr Phe Phe Ser Ser Glu Phe Ile Asn Asn Val Asn Lys Pro
    130
                        135
                                             140
Val Gln Ala Ala Leu Phe Val Ser Trp Ile Gln Gln Val Leu Val Asp
                    150
                                        155
Phe Thr Thr Glu Ala Asn Gln Lys Ser Thr Val Asp Lys Ile Ala Asp
                165
                                    170
Ile Ser Ile Val Val Pro Tyr Ile Gly Leu Ala Leu Asn Ile Gly Asn
            180
                                185
Glu Ala Gln Lys Gly Asn Phe Lys Asp Ala Leu Glu Leu Leu Gly Ala
                            200
Gly Ile Leu Leu Glu Phe Glu Pro Glu Leu Leu Ile Pro Thr Ile Leu
                        215
                                            220
Val Phe Thr Ile Lys Ser Phe Leu Gly Ser Ser Asp Asn Lys Asn Lys
                    230
                                        235
Val Ile Lys Ala Ile Asn Asn Ala Leu Lys Glu Arg Asp Glu Lys Trp
                245
                                    250
Lys Glu Val Tyr Ser Phe Ile Val Ser Asn Trp Met Thr Lys Ile Asn
                                265
Thr Gln Phe Asn Lys Arg Lys Glu Gln Met Tyr Gln Ala Leu Gln Asn
                            280
Gln Val Asn Ala Ile Lys Thr Ile Ile Glu Ser Lys Tyr Asn Ser Tyr
                        295
                                            300
Thr Leu Glu Glu Lys Asn Glu Leu Thr Asn Lys Tyr Asp Ile Lys Gln
                    310
                                        315
Ile Glu Asn Glu Leu Asn Gln Lys Val Ser Ile Ala Met Asn Asn Ile
                325
                                    330
Asp Arg Phe Leu Thr Glu Ser Ser Ile Ser Tyr Leu Met Lys Leu Ile
                                345
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Asn Glu Val Lys Ile Asn Lys Leu Arg Glu Tyr Asp Glu Asn Val Lys

360

355

<210> 29 <211> 1227 <212> DNA <213> Artificial Sequence <220> <223> Synthetic construct based on BoNTA Hc <221> CDS <222> (1)...(1224) <400> 29 atg gcc cca cca cgt ctg tgt att aga gtc aac aac tca gaa tta ttc Met Ala Pro Pro Arg Leu Cys Ile Arg Val Asn Asn Ser Glu Leu Phe ttt gtc gct tcc gag tca agc tac aac gag aac gat att aac aca cct 96 Phe Val Ala Ser Glu Ser Ser Tyr Asn Glu Asn Asp Ile Asn Thr Pro 2.0 aaa gag att gac gat act acc aac cta aac aac tac cgg aac aac 144 Lys Glu Ile Asp Asp Thr Thr Asn Leu Asn Asn Tyr Arg Asn Asn 40 ttg gat gag gtt att ttg gat tac aac tca cag acc atc cct caa att 192 Leu Asp Glu Val Ile Leu Asp Tyr Asn Ser Gln Thr Ile Pro Gln Ile 50 55 tcc aac cgt acc tta aac act ctt gtc caa gac aac tcc tac gtt cca 240 Ser Asn Arg Thr Leu Asn Thr Leu Val Gln Asp Asn Ser Tyr Val Pro 65 70 aga tac gat tot aac ggt acc toa gag atc gag gag tat gat gtt gtt 288 Arg Tyr Asp Ser Asn Gly Thr Ser Glu Ile Glu Glu Tyr Asp Val Val 85 95 gac ttt aac gtc ttt ttc tat ttg cat gcc cag aag gtg cca gaa ggt 336 Asp Phe Asn Val Phe Phe Tyr Leu His Ala Gln Lys Val Pro Glu Gly 100 gaa acc aac atc tca ttg act tct tcc att gat acc gcc ttg ttg gaa 384 Glu Thr Asn Ile Ser Leu Thr Ser Ser Ile Asp Thr Ala Leu Leu Glu 115 120 gag tee aag gat ate tte ttt tet teg gag ttt ate gat act ate aac 432 Glu Ser Lys Asp Ile Phe Phe Ser Ser Glu Phe Ile Asp Thr Ile Asn 135 aag cct gtc aac gcc gct ctg ttc att gat tgg att agc aag gtc atc 480 Lys Pro Val Asn Ala Ala Leu Phe Ile Asp Trp Ile Ser Lys Val Ile 145 150 155 160 aga gat ttt acc act gaa gct act caa aag tcc act gtt gat aag att 528

	Arg	Asp	Phe	Thr	Thr 165	Glu	Ala	Thr	Gln	Lys 170	Ser	Thr	Val	Asp	Lys 175	Ile	
	_	_			_		_		tat Tyr 185	_			_	_			576
						_			ttt Phe			_		_	_	_	624
									gtt Val								672
									tac Tyr								720
									aac Asn								768
									att Ile 265								816
\									aag Lys								864
									act Thr								912
									aga Arg								960
	aac Asn	aac Asn	att Ile	gaa Glu	gaa Glu 325	gag Glu	ttg Leu	aac Asn	aag Lys	aaa Lys 330	gtt Val	tct Ser	ttg Leu	gct Ala	atg Met 335	aag Lys	1008
									tcc Ser 345								1056
									aag Lys								1104
									att Ile								1152
	gga Gly	gag Glu	cag Gln	aca Thr	aac Asn	gag Glu	ctg Leu	agt Ser	gat Asp	ttg Leu	gtt Val	act Thr	tcc Ser	act Thr	ttg Leu	aac Asn	1200

385 390 395 400

tcc tcc att cca ttt gag ctt tct taa Ser Ser Ile Pro Phe Glu Leu Ser 405 1227

<210> 30

<211> 408

<212> PRT

<213> Artificial Sequence

<220>

<223> Encoded polypeptide of a synthetic construct based on BoNTF Hn

<400> 30

 Met Ala Pro Pro Arg Leu Cys
 Ile Arg Val Asn Asn Ser Glu Leu Phe

 1
 5
 10
 15

 Phe Val Ala Ser Glu Ser Ser Tyr Asn Glu Asn Asp Ile Asn Thr Pro
 20
 25
 30

 Lys Glu Ile Asp Asp Asp Thr Thr Asn Leu Asn Asn Asn Asn Tyr Arg Asn Asn
 35
 40
 45

 Leu Asp Glu Val Ile Leu Asp Tyr Asn Ser Gln Thr Ile Pro Gln Ile
 50
 55
 60

 Ser Asn Arg Thr Leu Asn Thr Leu Val Gln Asp Asn Ser Tyr Val Pro

Ser Asn Arg Thr Leu Asn Thr Leu Val Gln Asp Asn Ser Tyr Val Pro
65 70 75 80

Arg Tyr Asp Ser Asn Gly Thr Ser Glu Ile Glu Glu Tyr Asp Val Val 85 90 95

Asp Phe Asn Val Phe Phe Tyr Leu His Ala Gln Lys Val Pro Glu Gly
100 105 110

Glu Thr Asn Ile Ser Leu Thr Ser Ser Ile Asp Thr Ala Leu Leu Glu
115 120 125

Glu Ser Lys Asp Ile Phe Phe Ser Ser Glu Phe Ile Asp Thr Ile Asn
130 135 140

Lys Pro Val Asn Ala Ala Leu Phe Ile Asp Trp Ile Ser Lys Val Ile
145 150 155 160

Arg Asp Phe Thr Thr Glu Ala Thr Gln Lys Ser Thr Val Asp Lys Ile 165 170 175

Ala Asp Ile Ser Leu Ile Val Pro Tyr Val Gly Leu Ala Leu Asn Ile 180 185 190

Ile Ile Glu Ala Glu Lys Gly Asn Phe Glu Glu Ala Phe Glu Leu Leu
195 200 205

Gly Val Gly Ile Leu Leu Glu Phe Val Pro Glu Leu Thr Ile Pro Val 210 215 220

Ile Leu Val Phe Thr Ile Lys Ser Tyr Ile Asp Ser Tyr Glu Asn Lys 225 230 235 240

Asn Lys Ala Ile Lys Ala Ile Asn Asn Ser Leu Ile Glu Arg Glu Ala
245 250 255

Lys Trp Lys Glu Ile Tyr Ser Trp Ile Val Ser Asn Trp Leu Thr Arg 260 265 270

Ile Asn Thr Gln Phe Asn Lys Arg Lys Glu Gln Met Tyr Gln Ala Leu
275 280 285

Gln Asn Gln Val Asp Ala Ile Lys Thr Ala Ile Glu Tyr Lys Tyr Asn 290 295 300

Asn Tyr Thr Ser Asp Glu Lys Asn Arg Leu Glu Ser Glu Tyr Asn Ile 305 310 315 320



Asn Asn Ile Glu Glu Leu Asn Lys Lys Val Ser Leu Ala Met Lys 325 330 Asn Ile Glu Arg Phe Met Thr Glu Ser Ser Ile Ser Tyr Leu Met Lys Leu Ile Asn Glu Ala Lys Val Gly Lys Leu Lys Lys Tyr Asp Asn His 360 Val Lys Ser Asp Leu Leu Asn Tyr Ile Leu Asp His Arg Ser Ile Leu 375 380 Gly Glu Gln Thr Asn Glu Leu Ser Asp Leu Val Thr Ser Thr Leu Asn 390 395 Ser Ser Ile Pro Phe Glu Leu Ser 405 <210> 31 <211> 1233 <212> DNA <213> Artificial Sequence <223> Synthetic construct based on BoNTA Hc <221> CDS <222> (1) . . . (1230) <400> 31 atg gcc aaa aat acc ggt aaa tct gaa cag tgt att att gtt aat aat 48 Met Ala Lys Asn Thr Gly Lys Ser Glu Gln Cys Ile Ile Val Asn Asn 1 10 gag gat tta ttt ttc ata gct aat aaa gat agt ttt tca aaa gat tta 96 Glu Asp Leu Phe Phe Ile Ala Asn Lys Asp Ser Phe Ser Lys Asp Leu 20 25 gct aaa gca gaa act ata gca tat aat aca caa aat aat act ata gaa 144 Ala Lys Ala Glu Thr Ile Ala Tyr Asn Thr Gln Asn Asn Thr Ile Glu 35 40 aat aat ttt tct ata gat cag ttg att tta gat aat gat tta agc agt 192 Asn Asn Phe Ser Ile Asp Gln Leu Ile Leu Asp Asn Asp Leu Ser Ser 50 ggc ata gac tta cca aat gaa aac aca gaa cca ttt aca aat ttt gac 240 Gly Ile Asp Leu Pro Asn Glu Asn Thr Glu Pro Phe Thr Asn Phe Asp 65 gac ata gat atc cct gtg tat att aaa caa tct gct tta aaa aaa att 288 Asp Ile Asp Ile Pro Val Tyr Ile Lys Gln Ser Ala Leu Lys Lys Ile ttt gtg gat gga gat agc ctt ttt gaa tat tta cat gct caa aca ttt 336 Phe Val Asp Gly Asp Ser Leu Phe Glu Tyr Leu His Ala Gln Thr Phe 100 105 cct tct aat ata gaa aat cta caa cta acg aat tca tta aat gat gct 384 Pro Ser Asn Ile Glu Asn Leu Gln Leu Thr Asn Ser Leu Asn Asp Ala

120

125



115

	_					_					aac Asn		_	432
											aac Asn			480
		_		_	-			_			aaa Lys	_		528
											ata Ile 190			576
			_			_	_		-		aaa Lys		_	624
											cca Pro			672
											gta Val			720
											aaa Lys			768
)											tgg Trp 270			816
											tac Tyr			864
											gat Asp			912
											gat Asp			960
											ata Ile			1008
											atg Met 350			1056

atg att cca tta gct gta aaa aag tta aaa gac ttt gat gat aat ctt Met Ile Pro Leu Ala Val Lys Lys Leu Lys Asp Phe Asp Asp Asn Leu 355 360 aag aga gat tta ttg gag tat ata gat aca aat gaa cta tat tta ctt 1152 Lys Arg Asp Leu Leu Glu Tyr Ile Asp Thr Asn Glu Leu Tyr Leu Leu 370 375 380 gat gaa gta aat att cta aaa tca aaa gta aat aga cac cta aaa gac 1200 Asp Glu Val Asn Ile Leu Lys Ser Lys Val Asn Arg His Leu Lys Asp 385 390 agt ata cca ttt gat ctt tca cta tat acc taa 1233 Ser Ile Pro Phe Asp Leu Ser Leu Tyr Thr

<210> 32 <211> 410 <212> PRT <213> Artificial Sequence

<220>
<223> Encoded polypeptide of a synthetic construct based on BoNTG Hn

<400> 32 Met Ala Lys Asn Thr Gly Lys Ser Glu Gln Cys Ile Ile Val Asn Asn 10 Glu Asp Leu Phe Phe Ile Ala Asn Lys Asp Ser Phe Ser Lys Asp Leu Ala Lys Ala Glu Thr Ile Ala Tyr Asn Thr Gln Asn Asn Thr Ile Glu 40 Asn Asn Phe Ser Ile Asp Gln Leu Ile Leu Asp Asn Asp Leu Ser Ser Gly Ile Asp Leu Pro Asn Glu Asn Thr Glu Pro Phe Thr Asn Phe Asp 70 75 Asp Ile Asp Ile Pro Val Tyr Ile Lys Gln Ser Ala Leu Lys Lys Ile Phe Val Asp Gly Asp Ser Leu Phe Glu Tyr Leu His Ala Gln Thr Phe 100 Pro Ser Asn Ile Glu Asn Leu Gln Leu Thr Asn Ser Leu Asn Asp Ala 120 Leu Arg Asn Asn Lys Val Tyr Thr Phe Phe Ser Thr Asn Leu Val 135 140 Glu Lys Ala Asn Thr Val Val Gly Ala Ser Leu Phe Val Asn Trp Val 150 155 Lys Gly Val Ile Asp Asp Phe Thr Ser Glu Ser Thr Gln Lys Ser Thr 165 170 Ile Asp Lys Val Ser Asp Val Ser Ile Ile Ile Pro Tyr Ile Gly Pro 180 185 Ala Leu Asn Val Gly Asn Glu Thr Ala Lys Glu Asn Phe Lys Asn Ala 200 Phe Glu Ile Gly Gly Ala Ala Ile Leu Met Glu Phe Ile Pro Glu Leu Ile Val Pro Ile Val Gly Phe Phe Thr Leu Glu Ser Tyr Val Gly Asn 225 230 235

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Lys Gly His Ile Ile Met Thr Ile Ser Asn Ala Leu Lys Lys Arg Asp
                245
                                     250
Gln Lys Trp Thr Asp Met Tyr Gly Leu Ile Val Ser Gln Trp Leu Ser
                                265
Thr Val Asn Thr Gln Phe Tyr Thr Ile Lys Glu Arg Met Tyr Asn Ala
                            280
Leu Asn Asn Gln Ser Gln Ala Ile Glu Lys Ile Ile Glu Asp Gln Tyr
                        295
                                             300
Asn Arg Tyr Ser Glu Glu Asp Lys Met Asn Ile Asn Ile Asp Phe Asn
                    310
                                         315
Asp Ile Asp Phe Lys Leu Asn Gln Ser Ile Asn Leu Ala Ile Asn Asn
                325
                                     330
Ile Asp Asp Phe Ile Asn Gln Cys Ser Ile Ser Tyr Leu Met Asn Arg
                                345
Met Ile Pro Leu Ala Val Lys Lys Leu Lys Asp Phe Asp Asp Asn Leu
                            360
                                                 365
Lys Arg Asp Leu Leu Glu Tyr Ile Asp Thr Asn Glu Leu Tyr Leu Leu
                        375
                                             380
Asp Glu Val Asn Ile Leu Lys Ser Lys Val Asn Arg His Leu Lys Asp
                    390
                                         395
Ser Ile Pro Phe Asp Leu Ser Leu Tyr Thr
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atc atc tac aac ggt cgt tac cag aac ttc tct atc tct ttc tgg gtt

	Ile	Ile 80	Tyr	Asn	Gly	Arg	Tyr 85	Gln	Asn	Phe	Ser	Ile 90	Ser	Phe	Trp	Val	
							aac Asn		_		_			_			339
							aac Asn									_	387
							tgg Trp		_	_	_		-				435
							tac Tyr										483
							gtt Val 165						-	_			531
Ø							ggt Gly										579
\bigcup							gtt Val										627
							tac Tyr										675
							act Thr										723
							aaa Lys 245										771
							ctg Leu										819
							ctg Leu										867
							tct Ser										915
							ggt Gly										963



305 310 315

ttc gta cgt aaa aac gac ctg gct tac atc aac gtt gtt gac cgt gac 1011 Phe Val Arg Lys Asn Asp Leu Ala Tyr Ile Asn Val Val Asp Arg Asp 325 gtt gaa tac cgt ctg tac gct gac atc tct atc gct aaa ccg gaa aaa 1059 Val Glu Tyr Arg Leu Tyr Ala Asp Ile Ser Ile Ala Lys Pro Glu Lys 335 345 atc atc aaa ctg atc cgt act tct aac tct aac acc tct ctg ggt cag 1107 Ile Ile Lys Leu Ile Arg Thr Ser Asn Ser Asn Ser Leu Gly Gln 355 360 365 atc atc gtt atg gac tcg atc ggt aac aac tgc act atg aac ttc cag 1155 Ile Ile Val Met Asp Ser Ile Gly Asn Asn Cys Thr Met Asn Phe Gln 370 aac aac aac ggt ggt aac atc ggt ctg ctg ggt ttc cac tct aac aac 1203 . Asn Asn Asn Gly Gly Asn Ile Gly Leu Leu Gly Phe His Ser Asn Asn 390 ctg gtt gct tct tca tgg tac tac aac atc cgt aaa aac act tct 1251 Leu Val Ala Ser Ser Trp Tyr Tyr Asn Asn Ile Arg Lys Asn Thr Ser 410 tot aac ggt tgc ttc tgg tot ttc atc tct aaa gaa cac ggt tgg cag 1299 Ser Asn Gly Cys Phe Trp Ser Phe Ile Ser Lys Glu His Gly Trp Gln 420 425 gaa aac taagaattc 1314 Glu Asn

<210> 34

<211> 432

<212> PRT

<213> Artificial Sequence

<220>

<223> Encoded polypeptide of a synthetic construct based on BoNTF Hc

<400> 34

Met Ser Tyr Thr Asn Asp Lys Ile Leu Ile Leu Tyr Phe Asn Lys Leu 10

Tyr Lys Lys Ile Lys Asp Asn Ser Ile Leu Asp Met Arg Tyr Glu Asn 25

Asn Lys Phe Ile Asp Ile Ser Gly Tyr Gly Ser Asn Ile Ser Ile Asn 40

Gly Asp Val Tyr Ile Tyr Ser Thr Asn Arg Asn Gln Phe Gly Ile Tyr

Ser Ser Lys Pro Ser Glu Val Asn Ile Ala Gln Asn Asn Asp Ile Ile

Tyr Asn Gly Arg Tyr Gln Asn Phe Ser Ile Ser Phe Trp Val Arg Ile 90 95

Pro Lys Tyr Phe Asn Lys Val Asn Leu Asn Asn Glu Tyr Thr Ile Ile 100 105 Asp Cys Ile Arg Asn Asn Asn Ser Gly Trp Lys Ile Ser Leu Asn Tyr 120 Asn Lys Ile Ile Trp Thr Leu Gln Asp Thr Ala Gly Asn Asn Gln Lys 135 140 Leu Val Phe Asn Tyr Thr Gln Met Ile Ser Ile Ser Asp Tyr Ile Asn 150 155 Lys Trp Ile Phe Val Thr Ile Thr Asn Asn Arg Leu Gly Asn Ser Arg 165 170 Ile Tyr Ile Asn Gly Asn Leu Ile Asp Glu Lys Ser Ile Ser Asn Leu 185 Gly Asp Ile His Val Ser Asp Asn Ile Leu Phe Lys Ile Val Gly Cys 200 Asn Asp Thr Arg Tyr Val Gly Ile Arg Tyr Phe Lys Val Phe Asp Thr 215 220 Glu Leu Gly Lys Thr Glu Ile Glu Thr Leu Tyr Ser Asp Glu Pro Asp 230 235 Pro Ser Ile Leu Lys Asp Phe Trp Gly Asn Tyr Leu Leu Tyr Asn Lys 250 Arg Tyr Tyr Leu Leu Asn Leu Leu Arg Thr Asp Lys Ser Ile Thr Gln 260 265 Asn Ser Asn Phe Leu Asn Ile Asn Gln Gln Arg Gly Val Tyr Gln Lys 280 Pro Asn Ile Phe Ser Asn Thr Arg Leu Tyr Thr Gly Val Glu Val Ile 295 300 Ile Arg Lys Asn Gly Ser Thr Asp Ile Ser Asn Thr Asp Asn Phe Val 310 315 Arg Lys Asn Asp Leu Ala Tyr Ile Asn Val Val Asp Arg Asp Val Glu 325 330 Tyr Arg Leu Tyr Ala Asp Ile Ser Ile Ala Lys Pro Glu Lys Ile Ile 345 Lys Leu Ile Arg Thr Ser Asn Ser Asn Ser Leu Gly Gln Ile Ile 360 Val Met Asp Ser Ile Gly Asn Asn Cys Thr Met Asn Phe Gln Asn Asn 375 380 Asn Gly Gly Asn Ile Gly Leu Leu Gly Phe His Ser Asn Asn Leu Val 390 395 Ala Ser Ser Trp Tyr Tyr Asn Asn Ile Arg Lys Asn Thr Ser Ser Asn 405 410 Gly Cys Phe Trp Ser Phe Ile Ser Lys Glu His Gly Trp Gln Glu Asn 425 <210> 35

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<210> 35
<211> 1278
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic construct based on BoNTA Hc
<221> CDS
<222> (10)...(1269)
<400> 35
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Met Ile Leu Ile Ser Tyr Phe Asn Lys Phe Phe Lys Arg Ile 1 5 10

							aac Asn				_		_			_	99
						-	tcc Ser							_			147
							aac Asn							_	_		195
			_				caa Gln		_					-		_	243
							tct Ser 85			_	_					_	291
							aac Asn										339
`							tgg Trp										387
							aac Asn										435
							ggt Gly										483
	Phe	Val 160	Thr	Ile	Thr	Asn	gac Asp 165	Arg	Leu	Gly	Asp	Ser 170	Lys	Leu	Tyr	Ile	531
							caa Gln										579
	His	Val	Ser	Asp	Asn 195	Ile	tta Leu	Phe	Lys	Ile 200	Val	Asn	Cys	Ser	Tyr 205	Asn	627
	Arg	Tyr	Ile	Gly 210	Ile	Arg	tac Tyr	Phe	Asn 215	Ile	Phe	Asp	Lys	Glu 220	Leu	Asp	675
							tta Leu										723



							aac Asn 245										771
							cca Pro										819
				_			aac Asn		_	_					_		867
							aag Lys	_	-			_	_				915
							gtt Val										963
							cac His 325										1011
NA							acc Thr										1059
\bigcup	ttt Phe	aac Asn	caa Gln	gtc Val	gtc Val 355	gtt Val	atg Met	aac Asn	tcc Ser	gtc Val 360	ggt Gly	aac Asn	aac Asn	tgt Cys	acc Thr 365	atg Met	1107 -
							gga Gly										1155
							agt Ser										1203
	cac His	acc Thr 400	aac Asn	agc Ser	aat Asn	gga Gly	tgt Cys 405	ttt Phe	tgg Trp	aac Asn	ttt Phe	att Ile 410	tct Ser	gaa Glu	gaa Glu	cat His	1251
		tgg Trp		_		taa *	tagg	gato	:c								1278
	<211 <212)> 36 .> 41 !> PR	.9 !T	cial	Sea	n en c											

<220>

<213> Artificial Sequence

<400> 36 Met Ile Leu Ile Ser Tyr Phe Asn Lys Phe Phe Lys Arg Ile Lys Ser 1.0 Ser Ser Val Leu Asn Met Arg Tyr Lys Asn Asp Lys Tyr Val Asp Thr 25 Ser Gly Tyr Asp Ser Asn Ile Asn Ile Asn Gly Asp Val Tyr Lys Tyr 40 Pro Thr Asn Lys Asn Gln Phe Gly Ile Tyr Asn Asp Lys Leu Thr Glu Leu Asn Ile Ser Gln Asn Asp Tyr Ile Ile Tyr Asp Asn Lys Tyr Lys Asn Phe Ser Ile Ser Phe Trp Val Arg Ile Pro Asn Tyr Asp Asn Lys 85 90 Ile Val Asn Val Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Arg Asp 105 Asn Asn Ser Gly Trp Lys Val Ser Leu Asn His Asn Glu Ile Ile Trp 120 Thr Leu Gln Asp Asn Ala Gly Ile Asn Gln Lys Leu Ala Phe Asn Tyr 135 140 Gly Asn Ala Asn Gly Ile Ser Asp Tyr Ile Asn Lys Trp Ile Phe Val 150 Thr Ile Thr Asn Asp Arg Leu Gly Asp Ser Lys Leu Tyr Ile Asn Gly 165 170 Asn Leu Ile Asp Gln Lys Ser Ile Leu Asn Leu Gly Asn Ile His Val 180 185 190 Ser Asp Asn Ile Leu Phe Lys Ile Val Asn Cys Ser Tyr Thr Arg Tyr 200 Ile Gly Ile Arg Tyr Phe Asn Ile Phe Asp Lys Glu Leu Asp Glu Thr 215 220 Glu Ile Gln Thr Leu Tyr Ser Asn Glu Pro Asn Thr Asn Ile Leu Lys 230 235 Asp Phe Trp Gly Asn Tyr Leu Leu Tyr Asp Lys Glu Tyr Tyr Leu Leu 245 250 Asn Val Leu Lys Pro Asn Asn Phe Ile Asp Arg Arg Lys Asp Ser Thr 265 Leu Ser Ile Asn Asn Ile Arg Ser Thr Ile Leu Leu Ala Asn Arg Leu 280 Tyr Ser Gly Ile Lys Val Lys Ile Gln Arg Val Asn Asn Ser Ser Thr 295 300 Asn Asp Asn Leu Val Arg Lys Asn Asp Gln Val Tyr Ile Asn Phe Val 310 315 Ala Ser Lys Thr His Leu Phe Pro Leu Tyr Ala Asp Thr Ala Thr Thr 325 330 Asn Lys Glu Lys Thr Ile Lys Ile Ser Ser Ser Gly Asn Arg Phe Asn 340 345 Gln Val Val Met Asn Ser Val Gly Asn Asn Cys Thr Met Asn Phe 360 365 Lys Asn Asn Asn Gly Asn Asn Ile Gly Leu Leu Gly Phe Lys Ala Asp 375 Thr Val Val Ala Ser Thr Trp Tyr Tyr Thr His Met Arg Asp His Thr 390 395 Asn Ser Asn Gly Cys Phe Trp Asn Phe Ile Ser Glu Glu His Gly Trp 410 Gln Glu Lys



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<210> 37
<211> 1338
<212> DNA
<213> Artificial Sequence
<223> Synthetic construct based on BoNTA Hc
<221> CDS
<222> (9)...(1325)
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         Met Ala Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Asn
atc atc aat acc tcc atc ctg aac ctg cgc tac gaa tcc aat cac ctg
Ile Ile Asn Thr Ser Ile Leu Asn Leu Arg Tyr Glu Ser Asn His Leu
 15
atc gac ctg tct cgc tac gct tcc aaa atc aac atc ggt tct aaa gtt
Ile Asp Leu Ser Arg Tyr Ala Ser Lys Ile Asn Ile Gly Ser Lys Val
                 35
                                                          45
aac ttc gat ccg atc gac aag aat cag atc cag ctg ttc aat ctg gaa
                                                                    194
Asn Phe Asp Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu
tct tcc aaa atc gaa gtt atc ctg aag aat gct atc gta tac aac tct
                                                                   242
Ser Ser Lys Ile Glu Val Ile Leu Lys Asn Ala Ile Val Tyr Asn Ser
         65
                             70
atg tac gaa aac ttc tcc acc tcc ttc tgg atc cgt atc ccg aaa tac
                                                                   290
Met Tyr Glu Asn Phe Ser Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr
                         85
ttc aac tcc atc tct ctg aac aat gaa tac acc atc atc aac tgc atg
                                                                   338
Phe Asn Ser Ile Ser Leu Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met
                    100
                                         105
gaa aac aat tot ggt tgg aaa gta tot otg aac tac ggt gaa atc atc
                                                                   386
Glu Asn Asn Ser Gly Trp Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile
                115
                                     120
                                                         125
tgg act ctg cag gac act cag gaa atc aaa cag cgt gtt gta ttc aaa
                                                                   434
Trp Thr Leu Gln Asp Thr Gln Glu Ile Lys Gln Arg Val Val Phe Lys
            130
tac tot cag atg atc aac atc tot gac tac atc aat cgc tgg atc tto
                                                                   482
Tyr Ser Gln Met Ile Asn Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe
        145
                            150
gtt acc atc acc aac aat cgt ctg aat aac tcc aaa atc tac atc aac
                                                                   530
Val Thr Ile Thr Asn Asn Arg Leu Asn Asn Ser Lys Ile Tyr Ile Asn
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160 165 170

			_	_	cag Gln 180		_								578
	-				atg Met						-	 _			626
	_				aaa Lys				_		_	_	_		674
	_		_		gac Asp	_		_		_					722
			_		ggt Gly	_		_	_		_	_			770
					gat Asp 260										818
\	_	_			atg Met					_	_		_	_	866
					ctg Leu										914
					gcg Ala										962
					atc Ile										1010
					tct Ser 340										1058
					gtt Val										1106
					ggt Gly										1154
					gat Asp										1202

aat atc gct aaa ctg gtt gct tcc aac tgg tac aat cgt cag atc gaa
Asn Ile Ala Lys Leu Val Ala Ser Asn Trp Tyr Asn Arg Gln Ile Glu
400

cgt tcc tct cgc act ctg ggt tgc tct tgg gag ttc atc ccg gtt gat
Arg Ser Ser Arg Thr Leu Gly Cys Ser Trp Glu Phe Ile Pro Val Asp
415

gac ggt tgg ggt gaa cgt ccg ctg taa cccgggaaag ctt
Asp Gly Trp Gly Glu Arg Pro Leu *

<210> 38 <211> 415 <212> PRT <213> Clostridium botulinum

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290
                         295
                                             300
Val Lys Asn Lys Glu Tyr Arg Leu Ala Thr Asn Ala Ser Gln Ala Gly
                    310
                                         315
Val Glu Lys Ile Leu Ser Ala Leu Glu Ile Pro Asp Val Gly Asn Leu
                                     330
Ser Gln Val Val Wat Lys Ser Lys Asn Asp Gln Gly Ile Thr Asn
            340
                                 345
Lys Cys Lys Met Asn Leu Gln Asp Asn Asn Gly Asn Asp Ile Gly Phe
                            360
Ile Gly Phe His Gln Phe Asn Asn Ile Ala Lys Leu Val Ala Ser Asn
                        375
Trp Tyr Asn Arg Gln Ile Glu Arg Ser Ser Arg Thr Leu Gly Cys Ser
                    390
Trp Glu Phe Ile Pro Val Asp Asp Gly Trp Gly Glu Arg Pro Leu
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<210> 39
<211> 1348
<212> DNA
<213> Artificial Sequence
<220>
<223> Synthetic construct based on BoNTB Hc
<221> CDS
<222> (1) ... (1323)
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ctg cgt tac aaa gac aac aat ctg atc gat ctg tct ggt tac ggt gct
Leu Arg Tyr Lys Asp Asn Asn Leu Ile Asp Leu Ser Gly Tyr Gly Ala
aaa gtt gaa gta tac gac ggt gtt gaa ctg aat gac aag aac cag ttc
                                                                   144
Lys Val Glu Val Tyr Asp Gly Val Glu Leu Asn Asp Lys Asn Gln Phe
aaa ctg acc tct tcc gct aac tct aag atc cgt gtt act cag aat cag
                                                                   192
Lys Leu Thr Ser Ser Ala Asn Ser Lys Ile Arg Val Thr Gln Asn Gln
     50
                         55
aac atc atc ttc aac tcc gta ttc ctg gac ttc tct gtt tcc ttc tgg
                                                                   240
Asn Ile Ile Phe Asn Ser Val Phe Leu Asp Phe Ser Val Ser Phe Trp
 65
                     70
atc cgt atc ccg aaa tac aag aac gac ggt atc cag aat tac atc cac
                                                                   288
Ile Arg Ile Pro Lys Tyr Lys Asn Asp Gly Ile Gln Asn Tyr Ile His
                 85
aat gaa tac acc atc acc tgc atg aag aat aac tct ggt tgg aag
Asn Glu Tyr Thr Ile Ile Asn Cys Met Lys Asn Asn Ser Gly Trp Lys
            100
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					ggt Gly											aac Asn	384
		_			tct Ser	_			_				-	_	_		432
					aat Asn												480
					atc Ile 165												528
					cgt Arg												576
γQ_{i}					atc Ile												624
					acc Thr	_			_				_	_			672
					tac Tyr												720
					aaa Lys 245												768
					ctg Leu												816
					aac Asn							Asn					864
					aag Lys												912
	atc Ile 305	aat Asn	gat Asp	gac Asp	atc Ile	gta Val 310	cgt Arg	aaa Lys	gaa Glu	gac Asp	tac Tyr 315	atc Ile	tac Tyr	ctg Leu	gac Asp	ttc Phe 320	960
	ttc Phe	aac Asn	ctg Leu	aat Asn	cag Gln 325	gaa Glu	tgg Trp	cgt Arg	gta Val	tac Tyr 330	acc Thr	tac Tyr	aag Lys	tac Tyr	ttc Phe 335	aag Lys	1008
	aaa	gaa	gaa	gaa	aag	ctt	ttc	ctg	gct	ccg	atc	tct	gat	tcc	gac	gaa	1056

Lys	Glu	Glu	Glu 340	Lys	Leu	Phe	Leu	Ala 345	Pro	Ile	Ser	Asp	Ser 350	Asp	Glu	
	tac Tyr															1104
	tgc Cys 370															1152
	ctg Leu															1200
	tac Tyr															1248
	cgc Arg															1296
	aaa Lys							tag *	taad	cctct	ag a	agtcg	gaggo	cc		1343
tgca	ag															1348
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		ostr	idiu	ım bo	tuli	num										
<400	0> 40		idiu	ım bo	tuli	num										
	0> 40 Asn)					Ile	Leu	Asn 10	Asn	Ile	Ile	Leu	Asn 15	Leu	
Phe 1) Lys	Tyr	Asn 5	Ser	Glu			10					15		
Phe 1 Arg	Asn	Lys	Tyr Asp 20	Asn 5 Asn	Ser Asn	Glu Leu	Ile	Asp 25	10 Leu	Ser	Gly	Tyr	Gly 30	15 Ala	Lys	
Phe 1 Arg Val	Asn Tyr	Lys Lys Val 35	Tyr Asp 20 Tyr	Asn 5 Asn Asp	Ser Asn Gly	Glu Leu Val	Ile Glu 40	Asp 25 Leu	10 Leu Asn	Ser Asp	Gly Lys	Tyr Asn 45	Gly 30 Gln	15 Ala Phe	Lys Lys	
Phe 1 Arg Val Leu	Asn Tyr Glu Thr	Lys Lys Val 35 Ser	Tyr Asp 20 Tyr Ser	Asn 5 Asn Asp Ala	Ser Asn Gly Asn	Glu Leu Val Ser 55	Ile Glu 40 Lys	Asp 25 Leu Ile	10 Leu Asn Arg	Ser Asp Val Ser	Gly Lys Thr 60	Tyr Asn 45 Gln	Gly 30 Gln Asn	15 Ala Phe Gln	Lys Lys Asn Ile	
Phe 1 Arg Val Leu Ile 65	Asn Tyr Glu Thr	Lys Lys Val 35 Ser	Tyr Asp 20 Tyr Ser Asn	Asn 5 Asn Asp Ala Ser Tyr	Ser Asn Gly Asn Val 70	Glu Leu Val Ser 55 Phe	Ile Glu 40 Lys Leu	Asp 25 Leu Ile Asp	10 Leu Asn Arg Phe Ile	Ser Asp Val Ser 75	Gly Lys Thr 60 Val	Tyr Asn 45 Gln Ser	Gly 30 Gln Asn	15 Ala Phe Gln Trp His	Lys Lys Asn Ile 80	
Phe 1 Arg Val Leu Ile 65 Arg	Asn Tyr Glu Thr 50 Ile	Lys Lys Val 35 Ser Phe	Tyr Asp 20 Tyr Ser Asn Lys Ile	Asn 5 Asn Asp Ala Ser Tyr 85	Ser Asn Gly Asn Val 70 Lys	Glu Leu Val Ser 55 Phe	Ile Glu 40 Lys Leu Asp	Asp 25 Leu Ile Asp Gly Lys	10 Leu Asn Arg Phe Ile 90	Ser Asp Val Ser 75 Gln	Gly Lys Thr 60 Val	Tyr Asn 45 Gln Ser Tyr	Gly 30 Gln Asn Phe Ile Trp	15 Ala Phe Gln Trp His 95	Lys Lys Asn Ile 80 Asn	
Phe 1 Arg Val Leu Ile 65 Arg Glu	Asn Tyr Glu Thr 50 Ile	Lys Val 35 Ser Phe Pro Thr	Tyr Asp 20 Tyr Ser Asn Lys Ile 100	Asn 5 Asn Asp Ala Ser Tyr 85 Ile	Ser Asn Gly Asn Val 70 Lys Asn	Glu Leu Val Ser 55 Phe Asn Cys	Ile Glu 40 Lys Leu Asp Met Trp	Asp 25 Leu Ile Asp Gly Lys 105	10 Leu Asn Arg Phe Ile 90 Asn	Ser Asp Val Ser 75 Gln Asn	Gly Lys Thr 60 Val Asn Ser	Tyr Asn 45 Gln Ser Tyr Gly Ile	Gly 30 Gln Asn Phe Ile Trp 110	15 Ala Phe Gln Trp His 95 Lys	Lys Lys Asn Ile 80 Asn	
Phe 1 Arg Val Leu Ile 65 Arg Glu Ser	Asn Tyr Glu Thr 50 Ile Ile Tyr Ile Lys	Lys Lys Val 35 Ser Phe Pro Thr Arg 115	Tyr Asp 20 Tyr Ser Asn Lys Ile 100 Gly	Asn 5 Asn Asp Ala Ser Tyr 85 Ile Asn	Ser Asn Gly Asn Val 70 Lys Asn Arg	Glu Leu Val Ser 55 Phe Asn Cys Ile Glu	Ile Glu 40 Lys Leu Asp Met Trp 120	Asp 25 Leu Ile Asp Gly Lys 105 Thr	10 Leu Asn Arg Phe Ile 90 Asn Leu	Ser Asp Val Ser 75 Gln Asn Ile	Gly Lys Thr 60 Val Asn Ser Asp Glu	Tyr Asn 45 Gln Ser Tyr Gly Ile 125	Gly 30 Gln Asn Phe Ile Trp 110 Asn	15 Ala Phe Gln Trp His 95 Lys	Lys Lys Asn Ile 80 Asn Ile	
Phe 1 Arg Val Leu Ile 65 Arg Glu Ser Thr	Asn Tyr Glu Thr 50 Ile Ile Tyr Ile	Lys Lys Val 35 Ser Phe Pro Thr Arg 115 Ser	Tyr Asp 20 Tyr Ser Asn Lys Ile 100 Gly Val	Asn 5 Asn Asp Ala Ser Tyr 85 Ile Asn Phe	Ser Asn Gly Asn Val 70 Lys Asn Arg	Glu Leu Val Ser 55 Phe Asn Cys Ile Glu 135	Ile Glu 40 Lys Leu Asp Met Trp 120 Tyr	Asp 25 Leu Ile Asp Gly Lys 105 Thr	10 Leu Asn Arg Phe Ile 90 Asn Leu Ile	Ser Asp Val Ser 75 Gln Asn Ile Arg	Gly Lys Thr 60 Val Asn Ser Asp Glu 140	Tyr Asn 45 Gln Ser Tyr Gly Ile 125 Asp	Gly 30 Gln Asn Phe Ile Trp 110 Asn	15 Ala Phe Gln Trp His 95 Lys Gly Ser	Lys Lys Asn Ile 80 Asn Ile Lys Glu	

Asp Ile Arg Glu Val Ile Ala Asn Gly Glu Ile Ile Phe Lys Leu Asp 185 Gly Asp Ile Asp Arg Thr Gln Phe Ile Trp Met Lys Tyr Phe Ser Ile 200 Phe Asn Thr Glu Leu Ser Gln Ser Asn Ile Glu Glu Arg Tyr Lys Ile 215 Gln Ser Tyr Ser Glu Tyr Leu Lys Asp Phe Trp Gly Asn Pro Leu Met 235 Tyr Asn Lys Glu Tyr Tyr Met Phe Asn Ala Gly Asn Lys Asn Ser Tyr 245 250 Ile Lys Leu Lys Lys Asp Ser Pro Val Gly Glu Ile Leu Thr Arg Ser 265 Lys Tyr Asn Gln Asn Ser Lys Tyr Ile Asn Tyr Arg Asp Leu Tyr Ile 280 Gly Glu Lys Phe Ile Ile Arg Arg Lys Ser Asn Ser Gln Ser Ile Asn 295 300 Asp Asp Ile Val Arg Lys Glu Asp Tyr Ile Tyr Leu Asp Phe Phe Asn 310 315 Leu Asn Gln Glu Arg Val Tyr Thr Tyr Lys Phe Lys Lys Glu Glu Glu 325 330 Lys Leu Phe Leu Ala Pro Ile Ser Asp Ser Asp Glu Phe Tyr Asn Thr 340 345 Ile Gln Ile Lys Glu Tyr Asp Glu Gln Pro Thr Tyr Ser Cys Gln Leu 355 360 Leu Phe Lys Lys Asp Glu Glu Ser Thr Asp Glu Ile Gly Leu Ile Gly 375 Ile His Arg Phe Tyr Glu Ser Gly Ile Val Phe Glu Glu Tyr Lys Asp 390 Tyr Phe Cys Ile Ser Lys Trp Tyr Leu Lys Glu Val Lys Arg Lys Pro 405 410 Tyr Asn Leu Lys Leu Gly Cys Asn Trp Gln Phe Ile Pro Lys Asp Glu 425 Gly Trp Thr Glu 435 <210> 41 <211> 848 <212> PRT <213> Clostridium botulinum <400> 41 Ala Leu Asn Asp Leu Cys Ile Lys Val Asn Asn Trp Asp Leu Phe Phe 10 Ser Pro Ser Glu Asp Asn Phe Thr Asn Asp Leu Asn Lys Gly Glu Glu 25 Ile Thr Ser Asp Thr Asn Ile Glu Ala Ala Glu Glu Asn Ile Ser Leu 40 Asp Leu Ile Gln Gln Tyr Tyr Leu Thr Phe Asn Phe Asp Asn Glu Pro 55 Glu Asn Ile Ser Ile Glu Asn Leu Ser Ser Asp Ile Ile Gly Gln Leu 70 Glu Leu Met Pro Asn Ile Glu Arg Phe Pro Asn Gly Lys Lys Tyr Glu 90 Leu Asp Lys Tyr Thr Met Phe His Tyr Leu Arg Ala Gln Glu Phe Glu

100 105 110 His Gly Lys Ser Arg Ile Ala Leu Thr Asn Ser Val Asn Glu Ala Leu

Leu Asn Pro Ser Arg Val Tyr Thr Phe Phe Ser Ser Asp Tyr Val Lys Lys Val Asn Lys Ala Thr Glu Ala Ala Met Phe Leu Gly Trp Val Glu Gln Leu Val Tyr Asp Phe Thr Asp Glu Thr Ser Glu Val Ser Thr Thr Asp Lys Ile Ala Asp Ile Thr Ile Ile Pro Tyr Ile Gly Pro Ala Leu Asn Ile Gly Met Leu Tyr Lys Asp Asp Phe Val Gly Ala Leu Ile Phe Ser Gly Ala Val Ile Leu Leu Glu Phe Ile Pro Glu Ile Ala Ile Pro Val Leu Gly Thr Phe Ala Leu Val Ser Tyr Ile Ala Asn Lys Val Leu Thr Val Gln Thr Ile Asp Asn Ala Leu Ser Lys Arg Asn Glu Lys Trp Asp Glu Val Tyr Lys Tyr Ile Val Thr Asn Trp Leu Ala Lys Val Asn Thr Gln Ile Asp Leu Ile Arg Lys Lys Met Lys Glu Ala Leu Glu Asn Gln Ala Glu Ala Thr Lys Ala Ile Ile Asn Tyr Gln Tyr Asn Gln Tyr Thr Glu Glu Lys Asn Asn Ile Asn Phe Asn Ile Asp Asp Leu Ser Ser Lys Leu Asn Glu Ser Ile Asn Lys Ala Met Ile Asn Ile Asn Lys Phe Leu Asn Gln Cys Ser Val Ser Tyr Leu Met Asn Ser Met Ile Pro Tyr Gly Val Lys Arg Leu Glu Asp Phe Asp Ala Ser Leu Lys Asp Ala Leu Leu Lys Tyr Ile Arg Asp Asn Tyr Gly Thr Leu Ile Gly Gln Val Asp Arg Leu Lys Asp Lys Val Asn Asn Thr Leu Ser Thr Asp Ile Pro Phe Gln Leu Ser Lys Tyr Val Asp Asn Gln Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Asn Ile Ile Asn Thr Ser Ile Leu Asn Leu Arg Tyr Glu Ser Asn His Leu Ile Asp Leu Ser Arg Tyr Ala Ser Lys Ile Asn Ile Gly Ser Lys Val Asn Phe Asp Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu Ser Ser Lys Ile Glu Val Ile Leu Lys Asn Ala Ile Val Tyr Asn Ser Met Tyr Glu Asn Phe Ser Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr Phe Asn Ser Ile Ser Leu Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Glu Asn Asn Ser Gly Trp Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile Trp Thr Leu Gln Asp Thr Gln Glu Ile Lys Gln Arg Val Val Phe Lys Tyr Ser Gln Met Ile Asn Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe Val Thr Ile Thr Asn Asn Arg Leu Asn

Asn Ser Lys Ile Tyr Thr Ile Asn Gly Arg Leu Ile Asp Gln Lys Pro 585 Ile Ser Asn Leu Gly Asn Ile His Ala Ser Asn Asn Ile Met Phe Lys 600 Leu Asp Gly Cys Arg Asp Thr His Arg Tyr Ile Trp Ile Lys Tyr Phe 615 Asn Leu Phe Asp Lys Glu Leu Asn Glu Lys Glu Ile Lys Asp Leu Tyr 630 635 Asp Asn Gln Ser Asn Ser Gly Ile Leu Lys Asp Phe Trp Gly Asp Tyr 645 650 Leu Gln Tyr Asp Lys Pro Tyr Tyr Met Ile Leu Leu Tyr Asp Pro Asn 665 670 Lys Tyr Val Asp Val Asn Asn Val Gly Ile Arg Gly Tyr Met Tyr Leu 680 Lys Gly Pro Arg Gly Ser Val Met Thr Thr Asn Ile Tyr Leu Asn Ser 695 Ser Leu Tyr Arg Gly Thr Lys Phe Ile Ile Lys Lys Tyr Ala Ser Gly 710 715 Asn Lys Asp Asn Ile Val Arg Asn Asn Asp Arg Val Tyr Ile Asn Val 725 730 Val Val Lys Asn Lys Glu Tyr Arg Leu Ala Thr Asn Ala Ser Gln Ala 740 745 Gly Val Glu Lys Ile Leu Ser Ala Leu Glu Ile Pro Asp Val Gly Asn 755 760 Leu Ser Gln Val Val Wet Lys Ser Lys Asn Asp Gln Gly Ile Thr 775 780 Asn Lys Cys Lys Met Asn Leu Gln Asp Asn Asn Gly Asn Asp Ile Gly · 790 795 Phe Ile Gly Phe His Gln Phe Asn Asn Ile Ala Lys Leu Val Ala Ser 810 Asn Trp Tyr Asn Arg Gln Thr Glu Arg Ser Ser Arg Thr Leu Gly Cys 825 Ser Trp Glu Phe Ile Pro Val Asp Asp Gly Trp Gly Glu Arg Pro Leu

<210> 42 <211> 843

<212> PRT

<213> Clostridium botulinum

835

<400> 42

840

Tyr Ser Phe Phe Ser Met Asp Tyr Ile Lys Thr Ala Asn Lys Val Val Glu Ala Gly Leu Phe Ala Gly Trp Val Lys Gln Ile Val Asn Asp Phe Val Ile Glu Ala Asn Lys Ser Asn Thr Met Asp Lys Ile Ala Asp Ile Ser Leu Ile Val Pro Tyr Ile Gly Leu Ala Leu Asn Val Gly Asn Glu Thr Ala Lys Gly Asn Phe Glu Asn Ala Phe Glu Ile Ala Gly Ala Ser Ile Leu Leu Glu Phe Ile Pro Glu Leu Leu Ile Pro Val Val Gly Ala Phe Leu Leu Glu Ser Tyr Ile Asp Asn Lys Asn Lys Ile Ile Lys Thr Ile Asp Asn Ala Leu Thr Lys Arg Asn Glu Lys Trp Ser Asp Met Tyr Gly Leu Ile Val Ala Gln Trp Leu Ser Thr Val Asn Thr Gln Phe Tyr Thr Ile Lys Glu Gly Met Tyr Lys Ala Leu Asn Tyr Gln Ala Gln Ala Leu Glu Glu Ile Ile Lys Tyr Arg Tyr Asn Ile Tyr Ser Glu Lys Glu Lys Ser Asn Ile Asn Ile Asp Phe Asn Asp Ile Asn Ser Lys Leu Asn Glu Gly Ile Asn Gln Ala Ile Asp Asn Ile Asn Asn Phe Ile Asn Gly Cys Ser Val Ser Tyr Leu Met Lys Lys Met Ile Pro Leu Ala Val Glu Lys Leu Leu Asp Phe Asp Asn Thr Leu Lys Lys Asn Leu Leu Asn Tyr Ile Asp Glu Asn Lys Leu Tyr Leu Ile Gly Ser Ala Glu Tyr Glu Lys Ser Lys Val Asn Lys Tyr Leu Lys Thr Ile Met Pro Phe Asp Leu Ser Ile Tyr Thr Asn Asp Thr Ile Leu Ile Glu Met Phe Asn Lys Tyr Asn Ser Glu Ile Leu Asn Asn Ile Ile Leu Asn Leu Arg Tyr Lys Asp Asn Asn Leu Ile Asp Leu Ser Gly Tyr Gly Ala Lys Val Glu Val Tyr Asp Gly Val Glu Leu Asn Asp Lys Asn Gln Phe Lys Leu Thr Ser Ser Ala Asn Ser Lys Ile Arg Thr Gln Asn Gln Asn Ile Ile Phe Asn Ser Val Phe Leu Asp Phe Ser Val Ser Phe Trp Ile Arg Ile Pro Lys Tyr Lys Asn Asp Gly Ile Gln Asn Tyr Ile His Asn Glu Tyr Thr Ile Ile Asn Cys Met Lys Asn Asn Ser Gly Trp Lys Ile Ser Ile Arg Gly Arg Ile Ile Trp Thr Leu Ile Asp Ile Asn Gly Lys Thr Lys Ser Val Phe Phe Glu Tyr Asn Ile Arg Glu Asp Ile Ser Glu Tyr Ile Asn Arg Trp Phe Phe Val Thr Ile Thr Asn Asn Leu Asn Asn Ala Lys Ile Tyr Ile Asn

Q

Gly Lys Leu Glu Ser Asn Thr Asp Ile Lys Asp Ile Arg Glu Val Ile Ala Asn Gly Glu Ile Ile Phe Lys Leu Asp Gly Asp Ile Asp Arg Thr Gln Phe Ile Trp Met Lys Tyr Phe Ser Ile Phe Asn Thr Glu Leu Ser Gln Ser Asn Ile Glu Glu Arg Tyr Lys Ile Gln Ser Tyr Ser Glu Tyr Leu Lys Asp Phe Trp Gly Asn Pro Leu Met Tyr Asn Lys Glu Tyr Tyr Met Phe Asn Ala Gly Asn Lys Asn Ser Tyr Ile Lys Leu Lys Lys Asp Ser Pro Val Gly Glu Ile Leu Thr Arg Ser Lys Tyr Asn Gln Asn Ser Lys Tyr Ile Asn Tyr Arg Asp Leu Tyr Ile Gly Glu Lys Phe Ile Ile Arg Arg Lys Ser Asn Ser Gln Ser Ile Asn Asp Asp Ile Val Arg Lys Glu Asp Tyr Ile Tyr Leu Asp Phe Phe Asn Leu Asn Gln Glu Trp Arg Val Tyr Thr Tyr Lys Tyr Phe Lys Lys Glu Glu Leu Phe Leu Ala Pro Ile Ser Asp Ser Asp Glu Phe Tyr Asn Thr Ile Gln Ile Lys Glu Tyr Asp Glu Gln Pro Thr Tyr Ser Cys Gln Leu Leu Phe Lys Lys Asp Glu Glu Ser Thr Asp Glu Ile Gly Leu Ile Gly Ile His Arg Phe Tyr Glu Ser Gly Ile Val Phe Glu Glu Lys Asp Phe Cys Ile Ser Trp Tyr Leu Glu Val Lys Arg Lys Pro Tyr Asn Leu Lys Leu Gly Cys Asn Trp Gln Phe Ile Pro Lys Asp Glu Gly Trp Thr Glu